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DICTIONARY FILE UPDATES:   6 MAY 2009  HIGHEST RN 1143575-54-5

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=> file zcaplus
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FILE COVERS 1907 - 7 May 2009  VOL 150 ISS 19
FILE LAST UPDATED: 6 May 2009  (20090506/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED:  Feb 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE:  Feb 2009

ZCAplus now includes complete International Patent Classification (IPC)
reclassification data for the third quarter of 2008.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate
substance identification.
'OBI' IS DEFAULT SEARCH FIELD FOR 'ZCAPLUS' FILE
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=> d stat que L31
L15          246 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  DELSOLDATO P?/AU OR
                 DEL SOLDATO P?/AU
L16           54 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  SANTUS G?/AU
L17           13 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  L15 AND L16
L18          490 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  NITROOXY?/BI
L19          115 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  NITRO OXY?/BI
L20           32 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  (L15 OR L16) AND (L18
                 OR L19)
L23       87564 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  ?OXYGENAS?/BI
L24       33712 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  COX#/BI
L25           2 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  L17 AND (L23 OR L24)
L26          32 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  L20 OR L25
L28           5 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  L20 AND (L23 OR L24)
L29          32 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  L26 OR L28
L30          32 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  ?NITROOXY?/BI AND
                 (L15 OR L16)
L31          32 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  L29 OR L30


=> d ibib abs hitind L31 1-32

L31  ANSWER 1 OF 32  ZCAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:         2005:673257  ZCAPLUS  Full-text
DOCUMENT NUMBER:          143:153219
TITLE:                    Preparation of prostaglandin nitrooxy derivatives
                          for the treatment of glaucoma
INVENTOR(S):              Ongini, Ennio; Benedini, Francesca; Chiroli, Valerio;
                          Del Soldato, Piero
PATENT ASSIGNEE(S):       Nicox, S. A., Fr.
SOURCE:                   PCT Int. Appl., 82 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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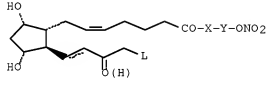
     WO 2005068421        A1    20050728    WO 2004-EP14820        20041227
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
             RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
             MR, NE, SN, TD, TG
     AU 2004313688        A1    20050728    AU 2004-313688         20041227
     CA 2551409           A1    20050728    CA 2004-2551409        20041227
     EP 1704141           A1    20060927    EP 2004-804405         20041227
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK,
             BA, HR, IS, YU
     CN 1906159           A     20070131    CN 2004-80039805       20041227
     BR 2004018245        A     20070417    BR 2004-18245          20041227
     JP 2007518716        T     20070712    JP 2006-546105         20041227
```

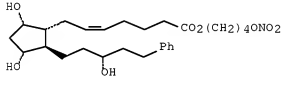
JP 3984283	B2	20071003			
US 20050272743	A1	20051208	US 2005-29698		20050105
US 7273946	B2	20070925			
IN 2006DN03240	A	20070824	IN 2006-DN3240		20060606
MX 2006007678	A	20060901	MX 2006-7678		20060704
KR 2006113753	A	20061102	KR 2006-713440		20060704
KR 850133	B1	20080804			
US 20080058392	A1	20080306	US 2007-841628		20070820
US 7449469	B2	20081111			
KR 2008007415	A	20080118	KR 2008-700325		20080104
KR 854838	B1	20080829			
US 20090030076	A1	20090129	US 2008-210975		20080915
PRIORITY APPLN. INFO.:			EP 2004-100001	A	20040105
			WO 2004-EP14820	W	20041227
			US 2005-29698	A1	20050105
			KR 2006-713440	A3	20060704
			US 2007-841628	A1	20070820

OTHER SOURCE(S): CASREACT 143:153219; MARPAT 143:153219

GI



I



II

AB Prostaglandin nitrooxy derivs. of formula I [L = benzyl, 3-(trifluoromethyl)phenoxy, 3-chlorophenoxy, (CH2)5Me; X = O, S, NH; Y = alkylene, cycloalkylene, phenylene, etc.] are prepared which have improved pharmacol. activity and enhanced tolerability. They can be employed for the treatment of glaucoma and ocular hypertension. Thus, II was prepared from 4-bromobutyl nitrate (preparation given) and latanoprost acid. The EC50 of II was 2.4 μM for cGMP formation in rat pheochromocytoma cells. Ophthalmic compns. containing I are described.

IC ICM C07C405-00
ICS A61P027-06; A61K031-5575

CC 26-3 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1, 63

ST prostaglandin nitrooxy prepn glaucoma treatment

IT Drug delivery systems
(emulsions, ophthalmic; preparation of prostaglandin nitrooxy derivs. for treatment of glaucoma)

IT Drug delivery systems
(ophthalmic; preparation of prostaglandin nitrooxy derivs. for treatment of glaucoma)

IT Antiglaucoma agents

Glaucoma (disease)
(preparation of prostaglandin nitrooxy derivs. for treatment of glaucoma)

IT Prostaglandins
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of prostaglandin nitrooxy derivs. for treatment of glaucoma)

IT Drug delivery systems
(solns., ophthalmic; preparation of prostaglandin nitrooxy derivs. for treatment of glaucoma)

IT Drug delivery systems
(suspensions, ophthalmic; preparation of prostaglandin nitrooxy derivs. for treatment of glaucoma)

IT 1044676-64-3 1044676-67-6 1044676-69-8 1044676-70-1 1044676-71-2
1044676-72-3 1044676-73-4 1044676-76-7 1044676-78-9 1044676-79-0
1044676-81-4 1044676-84-7 1044676-86-9
RL: PRPH (Prophetic)
(Preparation of prostaglandin nitrooxy derivatives for the treatment of glaucoma)

IT 860005-21-6P 860005-22-7P 860005-23-8P 860005-24-9P 860005-26-1P
860005-27-2P 860005-28-3P 860005-29-4P 860005-30-7P 860005-31-8P
860005-32-9P 860005-33-0P 860005-34-1P 860005-35-2P 860005-36-3P
860005-37-4P 860005-38-5P 860005-39-6P 860005-40-9P 860005-41-0P
860005-42-1P 860005-43-2P 860005-44-3P 860005-45-4P 860005-46-5P
860005-47-6P 860005-48-7P 860005-49-8P 860005-50-1P 860005-51-2P
860005-52-3P 860005-53-4P 860005-54-5P 860005-55-6P 860005-56-7P
860005-57-8P 860005-58-9P 860005-59-0P 860005-60-3P 860005-61-4P
860005-62-5P 860005-63-6P 860005-64-7P 860005-65-8P 860005-66-9P
860005-67-0P 860005-68-1P 860005-69-2P 860005-70-5P 860005-71-6P
860005-72-7P 860005-73-8P 860005-74-9P 860005-75-0P 860005-76-1P
860005-77-2P 860005-78-3P 860005-79-4P 860005-80-7P 860005-81-8P
860005-82-9P 860005-83-0P 860005-84-1P 860005-85-2P 860005-86-3P
860005-87-4P 860005-88-5P 860005-89-6P 860005-90-9P 860005-91-0P
860005-92-1P 860005-93-2P 860005-94-3P 860005-95-4P 860005-96-5P
860005-97-6P 860005-98-7P 860005-99-8P 860006-00-4P 860006-01-5P
860006-02-6P 860006-03-7P 860006-04-8P 860006-05-9P 860006-06-0P
860006-07-1P 860006-08-2P 860006-09-3P 860006-10-6P 860006-11-7P
860006-12-8P 860006-13-9P 860006-14-0P 860006-15-1P 860006-16-2P
860006-17-3P 860006-18-4P 860006-19-5P 860006-20-8P 860006-21-9P
860006-22-0P 860006-23-1P 860006-24-2P 860006-25-3P 860006-26-4P
860006-27-5P 860006-28-6P 860006-29-7P 860006-30-0P 860006-31-1P
860006-32-2P 860006-33-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of prostaglandin nitrooxy derivs. for treatment of glaucoma)

IT 109-99-9, Tetrahydrofuran, reactions 620-24-6, 3-(Hydroxymethyl)phenol 1135-24-6, Ferulic acid 4286-55-9 35421-08-0 41639-83-2, Latanoprost acid 71831-21-5, 4-(Bromomethyl)benzyl alcohol 475561-37-6 857465-38-4 1020165-81-4 1020165-82-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of prostaglandin nitrooxy derivs. for treatment of glaucoma)

IT 33036-62-3P 74597-04-9P 146563-40-8P 190442-16-1P 410071-23-7P 475561-36-5P 860006-34-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of prostaglandin nitrooxy derivs. for treatment of glaucoma)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 2 OF 32 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:523437 ZCAPLUS Full-text
DOCUMENT NUMBER: 143:59987
TITLE: A preparation of nitrooxy-derivatives of β-adrenergic blockers, useful for the treatment of hypertension and glaucoma
INVENTOR(S): Del Soldato, Piero; Benedini, Francesca; Ongini, Ennio
PATENT ASSIGNEE(S): Nicox S. A., Fr.
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005054218	A1	20050616	WO 2004-EP13682	20041201
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004295105	A1	20050616	AU 2004-295105	20041201
CA 2548127	A1	20050616	CA 2004-2548127	20041201
CN 1906182	A	20070131	CN 2004-80040927	20041201
EP 1748994	A1	20070207	EP 2004-803433	20041201
EP 1748994	B1	20090218		
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				
BR 2004017182	A	20070306	BR 2004-17182	20041201
JP 2007513113	T	20070524	JP 2006-541891	20041201
AT 423107	T	20090315	AT 2004-803433	20041201
KR 2006120164	A	20061124	KR 2006-710381	20060526
ZA 2006004463	A	20070425	ZA 2006-4463	20060531
MX 2006006251	A	20060809	MX 2006-6251	20060601
IN 2006CN01931	A	20070608	IN 2006-CN1931	20060601
US 20070060586	A1	20070315	US 2006-581450	20061004

PRIORITY APPLN. INFO.: EP 2003-104485 A 20031202
WO 2004-EP13682 W 20041201

OTHER SOURCE(S): CASREACT 143:59987
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to a preparation of nitrooxy-derivs. of β-adrenergic blockers and their use for the treatment of hypertension, cardiovascular diseases, glaucoma, migraine headache and vascular diseases. For instance, nitrooxy-derivative I (EC50 = 1.3 μM) was prepared via amidation of 4-(chloromethyl)benzoyl chloride by timolol hydrochloride (II•HCl), etherification. and subsequent nitration by AgNO3.

IC ICM C07D285-10
ICS A61K031-433; A61P009-00

CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

ST nitrooxy deriv prepn antihypertensive beta adrenergic blocker glaucoma antiglaucoma

IT Antiglaucoma agents
Antihypertensives
Cardiovascular agents
β-Adrenoceptor antagonists
(preparation of nitrooxy-derivs. of β-adrenergic blockers useful for the treatment of hypertension and glaucoma)

IT Blood vessel, disease
Cardiovascular system, disease
Glaucoma (disease)
Hypertension
(treatment of; preparation of nitrooxy-derivs. of β-adrenergic blockers useful for the treatment of hypertension and glaucoma)

IT 854028-32-3P 854028-33-4P 854028-34-5P 854028-35-6P 854028-36-7P 854028-37-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed; preparation of nitrooxy-derivs. of β-adrenergic blockers useful for the treatment of hypertension and glaucoma)

IT 854028-23-2P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of nitrooxy-derivs. of β-adrenergic blockers useful for the treatment of hypertension and glaucoma)

IT 854028-24-3P 854028-26-5P 854028-28-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of nitrooxy-derivs. of β-adrenergic blockers useful for the treatment of hypertension and glaucoma)

IT 876-08-4 1642-81-5, 4-Chloromethylbenzoic acid 18162-48-6 26839-75-8, Timolol 69267-58-9, Timolol hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of nitrooxy-derivs. of β-adrenergic blockers useful for the treatment of hypertension and glaucoma)

IT 854028-25-4P 854028-27-6P 854028-29-8P 854028-30-1P 854028-31-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of nitrooxy-derivs. of β-adrenergic blockers useful for the treatment of hypertension and glaucoma)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 3 OF 32 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:523280 ZCAPLUS Full-text
DOCUMENT NUMBER: 143:59817
TITLE: Preparation of nitrooxy derivatives of carvedilol and other β-blockers as antihypertensive drugs
INVENTOR(S): Del Soldato, Piero; Benedini, Francesca; Ongini, Ennio
PATENT ASSIGNEE(S): Nicox S. A., Fr.
SOURCE: PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005053685	A1	20050616	WO 2004-EP13683	20041201
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004294297	A1	20050616	AU 2004-294297	20041201
CA 2548129	A1	20050616	CA 2004-2548129	20041201
EP 1691804	A1	20060823	EP 2004-803434	20041201
EP 1691804	B1	20070404		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU				
CN 1886132	A	20061227	CN 2004-80035459	20041201
BR 2004016584	A	20070130	BR 2004-16584	20041201
AT 358478	T	20070415	AT 2004-803434	20041201
JP 2007513114	T	20070524	JP 2006-541892	20041201
ES 2285549	T3	20071116	ES 2004-803434	20041201
ZA 2006004458	A	20070425	ZA 2006-4458	20060331
KR 2006120677	A	20061127	KR 2006-710491	20060529
MX 2006006193	A	20060809	MX 2006-6193	20060601
US 20070072854	A1	20070329	US 2006-577912	20060913
PRIORITY APPLN. INFO.:			EP 2003-104484 A	20031202
			WO 2004-EP13683 W	20041201

OTHER SOURCE(S): CASREACT 143:59817; MARPAT 143:59817

AB Title compds. A(YONO2)s [s = 1, 2; A = R1CH(OZ)CH2NZ1R2; R1 = 1-naphthyloxymethyl, 4-(Me2CHOCH2CH2OCH2)C6H4OCH2, indol-4-yloxymethyl, carbazol-4-yloxymethyl, 4-MeSO2NHC6H4, etc.; R2 = CHMe2, CMe3, 2-MeOC6H4OCH2CH2, etc.; Z = H, CO, CO2, etc.; Z1 = H, CO; Y = (substituted) alkylene, cycloalkylene, etc.], were prepared Thus, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl][(6- nitrooxyhexanoyl)amino]]-2-propanol (preparation from carvedilol and 6-bromohexanoic acid described) increased cGMP levels in PC12 cells with EC50 = 0.6 μM.

IC ICM A61K031-403
ICS C07D209-88; C07C203-04; A61P009-12

CC 27-11 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 25, 63

IT Antihypertensives
Cardiovascular agents

Human
(preparation of nitrooxy derivs. of carvedilol and other β-blockers as antihypertensive drugs)

IT Cardiovascular system, disease
Glaucoma (disease)
Hypertension
(treatment; preparation of nitrooxy derivs. of carvedilol and other β-blockers as antihypertensive drugs)

IT 853906-47-5P 853906-48-6P 853906-49-7P 853906-50-0P 853906-51-1P
853906-52-2P 853906-53-3P 853906-54-4P 853906-55-5P 853906-56-6P
853906-57-7P 853906-58-8P 853906-59-9P 853906-60-2P 853906-61-3P
853906-62-4P 853906-63-5P 853906-64-6P 853906-65-7P 853906-66-8P
853906-67-9P 853906-68-0P 853906-69-1P 853906-70-4P 853906-71-5P
853906-72-6P 853906-73-7P 853906-74-8P 853906-75-9P 853906-76-0P
853906-77-1P 853906-78-2P 853906-79-3P 853906-80-6P 853906-81-7P
853906-82-8P 853906-83-9P 853906-84-0P 853906-85-1P 853906-86-2P
853906-87-3P 853906-88-4P 853906-89-5P 853906-90-8P 853906-91-9P
853906-92-0P 853906-93-1P 853906-94-2P 853906-95-3P 853906-96-4P
853906-97-5P 853906-98-6P 853906-99-7P 853907-00-3P 853907-01-4P
853907-02-5P 853907-03-6P 853907-04-7P 853907-05-8P 853907-06-9P
853907-07-0P 853907-08-1P 853907-09-2P 853907-10-5P 853907-11-6P
853907-12-7P 853907-13-8P 853907-14-9P 853907-15-0P 853907-16-1P
853907-17-2P 853907-18-3P 853907-19-4P 853907-20-7P 853907-21-8P
853907-22-9P 853907-23-0P 853907-24-1P 853907-25-2P 853907-26-3P
853907-27-4P 853907-28-5P 853907-29-6P 853907-30-9P 853907-31-0P
853907-32-1P 853907-33-2P 853907-34-3P 853907-35-4P 853907-36-5P
853907-37-6P 853907-38-7P 853907-39-8P 853907-40-1P 853907-41-2P
853907-42-3P 853907-43-4P 853907-44-5P 853907-45-6P 853907-46-7P
853907-47-8P 853907-48-9P 853907-49-0P 853907-50-3P 853907-51-4P
853907-52-5P 853907-53-6P 853907-54-7P 853907-55-8P 853907-56-9P
853907-57-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compound; preparation of nitrooxy derivs. of carvedilol and other β-blockers as antihypertensive drugs)

IT 7665-99-8, CGMP
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(level increasers; preparation of nitrooxy derivs. of carvedilol and other β-blockers as antihypertensive drugs)

IT 590-92-1, 3-Bromopropanoic acid 1642-81-5, 4-Chloromethylbenzoic acid
4224-70-8, 6-Bromohexanoic acid 72956-09-3, Carvedilol
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of nitrooxy derivs. of carvedilol and other β-blockers as antihypertensive drugs)

IT 853907-58-1P 853907-59-2P 853907-60-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of nitrooxy derivs. of carvedilol and other β-blockers as antihypertensive drugs)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 4 OF 32 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:120707 ZCAPLUS Full-text
DOCUMENT NUMBER: 142:191264
TITLE: Preparation of nitro derivatives of heterocyclic compounds as angiotensin II receptor blockers for therapeutic use

INVENTOR(S): Almirante, Nicoletta; Del Soldato, Piero; Ongini, Ennio
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005011646	A2	20050210	WO 2004-EP51550	20040720
WO 2005011646	A3	20050421		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004260830	A1	20050210	AU 2004-260830	20040720
CA 2534451	A1	20050210	CA 2004-2534451	20040720
EP 1653950	A2	20060510	EP 2004-766269	20040720
EP 1653950	B1	20080109		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
CN 1832742	A	20060913	CN 2004-80022483	20040720
BR 2004013028	A	20061003	BR 2004-13028	20040720
JP 2007500684	T	20070118	JP 2006-521571	20040720
AT 383155	T	20080115	AT 2004-766269	20040720
ES 2299861	T3	20080601	ES 2004-766269	20040720
AU 2005263655	A1	20060126	AU 2005-263655	20050202
CA 2574666	A1	20060126	CA 2005-2574666	20050202
WO 2006008196	A1	20060126	WO 2005-EP50459	20050202
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1778617	A1	20070502	EP 2005-707928	20050202
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				
CN 1984871	A	20070620	CN 2005-80024051	20050202
JP 2008506748	T	20080306	JP 2007-521923	20050202
KR 2006056352	A	20060524	KR 2006-701893	20060126
US 20060276523	A1	20061207	US 2006-566292	20060127
MX 2006001263	A	20060411	MX 2006-1263	20060131
IN 2006CN00674	A	20070608	IN 2006-CN674	20060223

NO 2006000900	A	20060224	NO 2006-900		20060224
US 20070238882	A1	20071011	US 2007-632666		20070117
IN 2007CN00727	A	20070824	IN 2007-CN727		20070220
PRIORITY APPLN. INFO.:			EP 2003-102379	A	20030731
			WO 2004-EP51550	W	20040720
			WO 2005-EP50459	W	20050202

OTHER SOURCE(S): CASREACT 142:191264; MARPAT 142:191264

AB Angiotensin II receptor blocker nitro derivs. of formula (I): R-(Y-ONO2)s (I) having wider pharmacol. activity and enhanced tolerability are claimed. They can be employed for treating cardiovascular, renal and chronic liver diseases and inflammatory processes.

IC ICM A61K031-00

CC 1-8 (Pharmacology)
Section cross-reference(s): 28

IT 76-83-5, Triphenylmethyl chloride 619-60-3, DMAP 627-18-9 771-61-9, Pentafluorophenol 927-58-2, 4-Bromobutanoyl chloride 1642-81-5, 4-(Chloromethyl)benzoic acid 2623-87-2, 4-Bromobutyric acid 4224-70-8, 6-Bromohexanoic acid 25952-53-8, 1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride 54894-16-5, 11-Nitrooxyundecanoic acid 63024-77-1, 3-(Chloromethyl)benzoyl chloride 83857-96-9, 2-Butyl-4-chloro-5-formylimidazole 104963-54-4, 4-Nitrooxybutanoic acid 114798-26-4 124750-51-2, N-(Triphenylmethyl)-5-(4'-bromomethylbiphenyl-2-yl-)tetrazole 124750-99-8, Losartan potassium 149968-28-5 258278-55-6, 4-(Nitrooxymethyl)benzoic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of nitro derivs. of heterocyclic compds. as angiotensin II receptor blockers for therapeutic use)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 5 OF 32 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:1124626 ZCAPLUS Full-text

DOCUMENT NUMBER: 142:79913

TITLE: Enalapril-nitroxy derivatives and related compounds as ace inhibitors for the treatment of cardiovascular diseases

INVENTOR(S): Almirante, Nicoletta; Ongini, Ennio; Del Soldato, Piero

PATENT ASSIGNEE(S): Nicox S. A., Fr.

SOURCE: PCT Int. Appl., 132 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004110432	A1	20041223	WO 2004-EP51089	20040611
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,				

SN, TD, TG

AU 2004246821	A1	20041223	AU 2004-246821		20040611
CA 2529478	A1	20041223	CA 2004-2529478		20040611
EP 1635816	A1	20060322	EP 2004-741779		20040611
EP 1635816	B1	20090304			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK					
BR 2004011430	A	20060725	BR 2004-11430		20040611
CN 1809345	A	20060726	CN 2004-80017127		20040611
AT 424199	T	20090315	AT 2004-741779		20040611
US 20050004100	A1	20050106	US 2004-869038		20040617
US 7217733	B2	20070515			
MX 2005013771	A	20060308	MX 2005-13771		20051215
KR 2006021900	A	20060308	KR 2005-724266		20051216
IN 2006CN00220	A	20070427	IN 2006-CN220		20060117
NO 2006000268	A	20060315	NO 2006-268		20060118
ZA 2006000526	A	20070131	ZA 2006-526		20060118
PRIORITY APPLN. INFO.:			EP 2003-101796	A	20030619
			WO 2004-EP51089	W	20040611

OTHER SOURCE(S): MARPAT 142:79913

AB Disclosure is compds. with a general formula of A-(X1-ONO2)S, wherein A is a known ACE-inhibitor such as enalapril and X1 is a spacer such as a (C1-C6)-alkylene. The compds. can be used as ACE-inhibitors for the treatment of cardiovascular and renal diseases and inflammatory processes. The compds. have an improved pharmacol. activity when compared with the structurally closest related prior art compound For example, synthesized N-[(1S)-1-ethoxycarbonyl-3-phenylpropyl]-L-alanyl-L-proline 3-nitrooxypropyl ester hydrogen maleate was found to have good vasorelaxation property.

IC ICM A61K031-401
ICS C07D207-16; A61P009-12

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 27

ST enalapril nitroxy deriv ACE inhibitor treatment cardiovascular disease; ethoxycarbonyl phenylpropyl alanylproline nitrooxypropyl maleate vasorelaxation

IT 50-78-2, Aspirin 50-78-2D, Aspirin, nitrooxy derivs.

811786-20-6	811786-21-7	811786-22-8	811786-23-9	811786-24-0
811786-25-1	811786-26-2	811786-27-3	811786-28-4	811786-29-5
811786-30-8	811786-32-0	811786-34-2	811786-36-4	811786-38-6
811786-40-0	811786-41-1	811786-43-3	811786-44-4	811786-45-5
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811786-51-3	811786-52-4	811786-53-5	811786-54-6	811786-55-7
811786-56-8	811786-58-0	811786-60-4	811786-61-5	811786-62-6
811786-63-7	811786-64-8	811786-65-9	811786-66-0	811786-67-1
811786-68-2	811786-69-3	811786-70-6	811786-71-7	811786-72-8
811786-73-9	811786-74-0	811786-75-1	811786-76-2	811786-77-3
811786-78-4	811786-79-5	811786-80-8	811786-81-9	811786-85-3
811786-86-4	811786-87-5	811786-88-6	811786-89-7	811786-90-0
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811787-05-0	811787-07-2	811787-09-4	811787-11-8	811787-13-0
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811787-25-4	811787-27-6	811787-29-8	811787-31-2	811787-33-4
811787-35-6	811787-38-9	811787-39-0	811787-40-3	811787-41-4
811787-42-5	811787-43-6	811787-44-7	811787-45-8	811787-46-9
811787-47-0	811787-48-1	811787-49-2	811787-50-5	811787-51-6
811787-52-7	811787-54-9	811787-55-0	811787-56-1	811787-57-2
811787-58-3	811787-60-7	811787-61-8	811787-63-0	811787-64-1
811787-66-3	811787-67-4	811787-68-5	811787-69-6	811787-70-9
811787-71-0	811787-72-1	811787-73-2	811787-74-3	811787-75-4

811787-77-6 811787-78-7 811787-79-8 811787-80-1 812681-82-6
812681-84-8 812681-85-9 812681-86-0 812681-87-1 812681-88-2
812681-89-3 812681-90-6 812681-91-7 812681-92-8 812681-93-9
812681-94-0 812681-95-1 812681-96-2 812681-97-3 812681-98-4
812681-99-5 812682-00-1 812682-01-2 812682-02-3 812682-03-4
812682-04-5 812682-05-6 812682-06-7 812682-07-8 812682-08-9
812682-09-0 812682-10-3 812682-11-4
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enalapril-nitroxy derivs. and related compound as ACE inhibitors for the treatment of cardiovascular and renal diseases)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

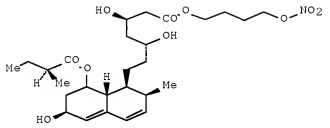
L31 ANSWER 6 OF 32 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:1059168 ZCAPLUS Full-text
DOCUMENT NUMBER: 142:38061
TITLE: Preparation of nitrooxy derivatives of fluvastatin, pravastatin, cerivastatin, atorvastatin and rosuvastatin as cholesterol-reducing agents with improved anti-inflammatory, antithrombotic and anti-platelet activity
INVENTOR(S): Benedini, Francesca; Ongini, Ennio; Del Soldato, Piero
PATENT ASSIGNEE(S): Nicox S. A., Fr.
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004105754	A1	20041209	WO 2004-EP50897	20040524
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 20050165084	A1	20050728	US 2004-849561	20040520
US 7166638	B2	20070123		
AU 2004243443	A1	20041209	AU 2004-243443	20040524
CA 2527168	A1	20041209	CA 2004-2527168	20040524
EP 1626716	A1	20060222	EP 2004-741636	20040524
EP 1626716	B1	20070207		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
BR 2004010049	A	20060425	BR 2004-10049	20040524
CN 1794987	A	20060628	CN 2004-80014498	20040524
AT 353214	T	20070215	AT 2004-741636	20040524
ES 2280978	T3	20070916	ES 2004-741636	20040524
ZA 2005009460	A	20070425	ZA 2005-9460	20051122
MX 2005012755	A	20060213	MX 2005-12755	20051125
IN 2005CN03560	A	20070525	IN 2005-CN3560	20051227
US 20070072942	A1	20070329	US 2006-590770	20061101

US 7297808	B2	20071120			
US 20080090857	A1	20080417	US 2007-905893		20071005
US 7462716	B2	20081209			
US 20080096908	A1	20080424	US 2007-905910		20071005
PRIORITY APPLN. INFO.:			EP 2003-101530	A	20030527
			US 2004-849561	A3	20040520
			WO 2004-EP50897	W	20040524
			US 2006-590770	A3	20061101

OTHER SOURCE(S): MARPAT 142:38061

GI



I

AB Nitrooxy derivs. of therapeutic agents, such as RCO-X-Y-ONO2 [RCO = acyl residue of therapeutic agents, including statin acids, such as fluvastatin, pravastatin, cerivastatin, atorvastatin and rosuvastatin, ACE inhibitors, angiotensin II receptor antagonists, β-adrenergic blockers, calcium channel blockers, antithrombotics and aspirin; X = O, S, NR1; Y = linking group, such as, alkylene or phenylene alone or in combination; R1 = H, alkyl], with improved pharmacol. activity and enhanced tolerability were prepared for therapeutic use in treating and/or preventing several diseases, in particular coronary syndromes and neurodegenerative disorders and autoimmune disorders , as well as for reducing cholesterol levels. The vascular disorders for treatment include acute coronary syndromes, stroke, peripheral vascular diseases, disorders associated with endothelial dysfunction, peripheral ischemia, vascular complications in diabetic patients and atherosclerosis. The neurodegenerative diseases for treatment include Alzheimer's disease, Parkinson's disease and multiple sclerosis. Thus, ester I was prepared via an esterification reaction of pravastatin sodium with 1,4-dibromobutane n DMF and subsequent treatment of the resulting 4-bromobutanyl pravastatin ester with silver nitrate in MeCN. The prepared nitrooxy statin derivs. were assayed for their ability to induce vasorelaxation, for their effect in vitro on inflammatory pathways, for activity on peripheral vascular disease, for effect on leukocyte adhesion, for antithrombotic activity, for anti-platelet activity, and for inhibition of tissue factor expression.

IC ICM A61K031-405
ICS A61K031-40; C07D209-26; C07D207-34; A61P003-06

CC 26-6 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1, 63

ST stroke treatment nitrooxy statin deriv prepn; Alzheimer disease treatment nitrooxy statin deriv prepn; endothelial dysfunction treatment nitrooxy statin deriv prepn; ischemia peripheral treatment nitrooxy statin deriv prepn; atherosclerosis treatment nitrooxy statin deriv prepn; Parkinson disease treatment nitrooxy statin deriv prepn; multiple sclerosis treatment nitrooxy statin deriv prepn; nitrooxy statin deriv

prepn cholesterol reducing agent; fluvastatin nitrooxy deriv prepn cholesterol reducing agent; cerivastatin nitrooxy deriv prepn cholesterol reducing agent; atorvastatin nitrooxy deriv prepn cholesterol reducing agent; rosuvastatin nitrooxy deriv prepn cholesterol reducing agent; pravastatin nitrooxy deriv prepn cholesterol reducing agent; coronary disease treatment nitrooxy statin deriv prepn; neurodegenerative disorder treatment nitrooxy statin deriv prepn; cholesterol level redn treatment nitrooxy statin deriv prepn; hypercholesterolemia treatment nitrooxy statin deriv prepn; drug delivery system nitrooxy statin prepn cholesterol reducing agent

IT Leukocyte
(adhesion, treatment; preparation of nitrooxy derivs. of fluvastatin, pravastatin, cerivastatin, atorvastatin and rosuvastatin as cholesterol-reducing agents with improved anti-inflammatory, antithrombotic and anti-platelet activity)

IT Artery, disease
(coronary, treatment; preparation of nitrooxy derivs. of fluvastatin, pravastatin, cerivastatin, atorvastatin and rosuvastatin as cholesterol-reducing agents with improved anti-inflammatory, antithrombotic and anti-platelet activity)

IT Nervous system, disease
(degeneration, treatment; preparation of nitrooxy derivs. of fluvastatin, pravastatin, cerivastatin, atorvastatin and rosuvastatin as cholesterol-reducing agents with improved anti-inflammatory, antithrombotic and anti-platelet activity)

IT Anti-inflammatory agents
(nonsteroidal; preparation of nitrooxy derivs. of fluvastatin, pravastatin, cerivastatin, atorvastatin and rosuvastatin as cholesterol-reducing agents with improved anti-inflammatory, antithrombotic and anti-platelet activity)

IT Blood vessel, disease
Ischemia
(peripheral, treatment; preparation of nitrooxy derivs. of fluvastatin, pravastatin, cerivastatin, atorvastatin and rosuvastatin as cholesterol-reducing agents with improved anti-inflammatory, antithrombotic and anti-platelet activity)

IT Anticholesteremic agents
Anticoagulants
Blood vessel, disease
Drug delivery systems
Human
(preparation of nitrooxy derivs. of fluvastatin, pravastatin, cerivastatin, atorvastatin and rosuvastatin as cholesterol-reducing agents with improved anti-inflammatory, antithrombotic and anti-platelet activity)

IT Brain, disease
(stroke, treatment; preparation of nitrooxy derivs. of fluvastatin, pravastatin, cerivastatin, atorvastatin and rosuvastatin as cholesterol-reducing agents with improved anti-inflammatory, antithrombotic and anti-platelet activity)

IT Alzheimer's disease
Atherosclerosis
Hypercholesterolemia
Inflammation
Multiple sclerosis
Parkinson's disease
Thrombosis
(treatment; preparation of nitrooxy derivs. of fluvastatin, pravastatin, cerivastatin, atorvastatin and rosuvastatin as cholesterol-reducing agents with improved anti-inflammatory,

antithrombotic and anti-platelet activity)
IT 803728-46-3P 803728-47-4P 803728-48-5P 803728-49-6P 803728-50-9P
803728-51-0P 803728-52-1P 803728-53-2P 803728-54-3P 803728-55-4P
803728-56-5P 803728-57-6P 803728-58-7P 803728-59-8P 803728-60-1P
803728-61-2P 803728-62-3P 803728-63-4P 803728-64-5P 803728-65-6P
803728-66-7P 803728-67-8P 803728-68-9P 803728-69-0P 803728-70-3P
803728-71-4P 803728-72-5P 803728-73-6P 803728-74-7P 803728-75-8P
803728-76-9P 803728-77-0P 803728-78-1P 803728-79-2P 803728-80-5P
803728-81-6P 803728-82-7P 803728-83-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(claimed compound; preparation of nitrooxy derivs. of fluvastatin,
pravastatin, cerivastatin, atorvastatin and rosuvastatin as
cholesterol-reducing agents with improved anti-inflammatory,
antithrombotic and anti-platelet activity)
IT 81093-37-0DP, Pravastatin, derivs. 93957-54-1DP, Fluvastatin, derivs.
134523-00-5DP, Atorvastatin, derivs. 145599-86-6DP, Cerivastatin,
derivs. 287714-41-4DP, Rosuvastatin, derivs. 733034-46-3P
733034-56-5P 803728-41-8P 803728-42-9P 803728-43-0P 803728-44-1P
803728-45-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(preparation of nitrooxy derivs. of fluvastatin, pravastatin,
cerivastatin, atorvastatin and rosuvastatin as cholesterol-reducing
agents with improved anti-inflammatory, antithrombotic and
anti-platelet activity)
IT 110-52-1, 1.4-Dibromobutane 612-12-4, α,α'-Dichloro-o-xylene
623-25-6, α,α'-Dichloro-p-xylene 626-16-4,
α,α'-Dichloro-m-xylene 81131-70-6, Pravastatin sodium
93957-55-2, Fluvastatin sodium 134523-03-8, Atorvastatin calcium
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of nitrooxy derivs. of fluvastatin, pravastatin,
cerivastatin, atorvastatin and rosuvastatin as cholesterol-reducing
agents with improved anti-inflammatory, antithrombotic and
anti-platelet activity)
IT 803728-85-0P 803728-86-1P 803728-87-2P 803728-88-3P 803728-89-4P
803728-90-7P 803728-91-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of nitrooxy derivs. of fluvastatin, pravastatin,
cerivastatin, atorvastatin and rosuvastatin as cholesterol-reducing
agents with improved anti-inflammatory, antithrombotic and
anti-platelet activity)
IT 57-88-5, Cholesterol, biological studies
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL
(Biological study)
(reducing; preparation of nitrooxy derivs. of fluvastatin,
pravastatin, cerivastatin, atorvastatin and rosuvastatin as
cholesterol-reducing agents with improved anti-inflammatory,
antithrombotic and anti-platelet activity)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 7 OF 32 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:723980 ZCAPLUS Full-text
DOCUMENT NUMBER: 141:236888
TITLE: The distinct alterations produced in cardiovascular

functions by prednisolone and nitro-prednisolone (NCX-1015) in the rat highlight a causal role for endothelin-1

AUTHOR(S): di Filippo, Clara; Rossi, Francesco; Ongini, Ennio; Del Soldato, Piero; Perretti, Mauro; D'Amico, Michele

CORPORATE SOURCE: Department of Experimental Medicine, Section of Pharmacology, 2nd University of Naples, Naples, Italy

SOURCE: Journal of Pharmacology and Experimental Therapeutics (2004), 310(3), 1133-1141
CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Daily administration of prednisolone, but not the derivative NCX-1015 (or prednisolone 21-[4'-nitrooxymethyl]benzoate), to rats resulted in a time- and dose-dependent increase in mean arterial blood pressure (MABP), significant after 1 wk for the dose of 6.9 μmol/kg i.p. ($n = 10$; $P < 0.05$), and 3 wk for the lower dose of 1.38 μmol/kg. A similar dichotomy of behavior was observed with respect to myocardial contractility and renal vascular resistance, in either case augmented by 3-wk treatment with prednisolone but not NCX-1015. In contrast, both NCX-1015 and prednisolone reduced plasma levels of corticosterone in a dose- (dose range of 0.69-6.9 μmol/kg i.p.) and time-dependent (1-3 wk) manner. Similar profiles were obtained for plasma nitrate values, although they were increased selectively after NCX-1015 administration. In contrast, prednisolone, but not NCX-1015, augmented plasma endothelin 1 (ET-1) with a profile that mirrored the changes observed in MABP and renal blood flow. Supply in the drinking water of the ET-1 receptor type A (ETA) antagonist FR139317 or mixed ETA/B, but not of selective ETB, antagonists prevented the changes produced by a 21-day treatment with prednisolone. In conclusion, this study indicates (1) a lack of occurrence of cardiovascular alterations by nitro-releasing derivative of prednisolone (NCX-1015), and (2) a functional link between prednisolone effects and the endogenous endothelin-1 system.

CC 2-4 (Mammalian Hormones)

REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 8 OF 32 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:608722 ZCAPLUS Full-text

DOCUMENT NUMBER: 141:150761

TITLE: The nitric oxide-releasing naproxen derivative displays cardioprotection in perfused rabbit heart submitted to ischemia-reperfusion

AUTHOR(S): Rossoni, Giuseppe; Manfredi, Barbara; Del Soldato, Piero; Berti, Ferruccio

CORPORATE SOURCE: Departments of Pharmacological Sciences and Pharmacology, Chemotherapy, and Medical Toxicology, University of Milan, Milan, Italy

SOURCE: Journal of Pharmacology and Experimental Therapeutics (2004), 310(2), 555-562
CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In this study, the pharmacol. activity of HCT-3012 [(S)-6-methoxy-α-methyl-2-naphtaleneacetic acid 4-(nitrooxy)butyl ester], a nitric oxide (NO)-releasing derivative of naproxen, was compared with that of naproxen in a model of acute

ischemia (40 min) and reperfusion (20 min) of the rabbit heart. HTC-3012 (3-100 μM), in spite of inhibition of 6-keto-prostaglandin Flα generation by the cardiac tissues, brought about a dose-dependent normalization of coronary perfusion pressure, associated with a reduction of ventricular contracture during ischemia with remarkable improvement of left ventricular developed pressure at reperfusion. These beneficial effects were accompanied by a substantial release of nitrite/nitrate in the heart perfusates, indicating that NO has been released by HCT-3012 and donated to the cardiac tissue. These events were paralleled by a significant reduction of creatine kinase activity in heart perfusates during reperfusion. Naproxen (10-100 μM) aggravated the myocardial damage in ischemic reperfused hearts, severely depressing the postischemic ventricular dysfunction. Perfusion of the heart with NG-monomethyl-l-arginine (10 μM) caused a marked aggravation of myocardial damage of the reperfused hearts, and this effect was dose dependently prevented by HCT-3012 but not by naproxen. The results of the present expts. clearly indicate that HCT-3012, by donating NO, displays a noticeable anti-ischemic effect in reperfused ischemic rabbit hearts. The safer gastrointestinal profile of HCT-3012 and its ability to control exptl. hypertension, suggest that this compound may have therapeutical potential in cardiovascular disease, namely in the prevention of myocardial ischemic events, and may represent a better alternative to conventional nonsteroidal anti-inflammatory drugs.

CC 1-8 (Pharmacology)

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 9 OF 32 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:545272 ZCAPLUS Full-text

DOCUMENT NUMBER: 141:139108

TITLE: Nitric Oxide Regulates Immune Cell Bioenergetic: A Mechanism to Understand Immunomodulatory Functions of Nitric Oxide-Releasing Anti-Inflammatory Drugs

AUTHOR(S): Fiorucci, Stefano; Mencarelli, Andrea; Distrutti, Eleonora; Baldoni, Monia; del Soldato, Piero; Morelli, Antonio

CORPORATE SOURCE: Dipartimento di Medicina Clinica e Sperimentale, Clinica di Gastroenterologia ed Epatologia, Universita degli Studi di Perugia, Perugia, Italy

SOURCE: Journal of Immunology (2004), 173(2), 874-882
CODEN: JOIMA3; ISSN: 0022-1767

PUBLISHER: American Association of Immunologists

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The 2-(acetyloxy)benzoic acid 3-(nitrooxymethyl)phenyl ester (NCX-4016) is a NO-releasing derivative of aspirin. In this study, the authors provide evidence that NCX-4016 delivered to PMBC-derived T lymphocytes and monocytes causes a transitory inhibition of cell respiration and ≈50% reduction of cellular ATP, which translates in a time-reversible inhibition of cell proliferation and IL-2, IL-4, IL-5, and IFN-γ secretion. Exposure of lymphocytes and monocytes to aspirin, 2-(acetyloxy)benzoic acid 3-(hydroxymethyl)phenyl ester (NCX-4017), a non-NO-releasing analog of NCX-4016, and cyclooxygenase inhibitors, reduced PG formation, but has no effect on cytokine/chemokine release. In contrast, delivering NO with (z)-1-[2-(2-aminoethyl)-N-(2-ammonio- ethyl)amino] diazen-1-ium-1,2 diolate (DETA-NO) reproduced most of the metabolic and anti-cytokine activities of NCX-4016. Scavenging NO with Hb or adding selective substrates of complex II, III, and IV of the mitochondrial respiratory chain reverses NCX-4016' inhibitory activities. Exposure to DETA-NO and NCX-4016 enhances glucose uptake, glycolytic rate, and lactate generation in CD3/CD28-costimulated lymphocytes, while reduced citric acid cycle intermediates. These effects were not

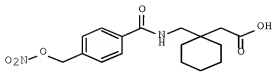
reproduced by selective and nonselective cyclooxygenase 2 inhibitors. In summary, the authors demonstrated that exposure of lymphocytes to NCX-4016 causes a metabolic hypoxia that inhibits lymphocyte reactivity to costimulatory mols., providing a potential counterregulatory mechanism to control activated immune system.

CC 15-10 (Immunochemistry)
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

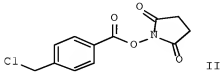
L31 ANSWER 10 OF 32 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:534167 ZCAPLUS Full-text
DOCUMENT NUMBER: 141:71285
TITLE: A preparation of nitrooxy-derivatives of carboxylic acids, useful as drugs for chronic pain
INVENTOR(S): Ongini, Ennio; Almirante, Nicoletta; Del Soldato, Piero
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004054965	A1	20040701	WO 2003-EP50932	20031203
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2510283	A1	20040701	CA 2003-2510283	20031203
AU 2003300252	A1	20040709	AU 2003-300252	20031203
EP 1572627	A1	20050914	EP 2003-799531	20031203
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1729160	A	20060201	CN 2003-80106668	20031203
JP 2006509822	T	20060323	JP 2004-560497	20031203
NZ 540345	A	20080530	NZ 2003-540345	20031203
RU 2340598	C2	20081210	RU 2005-122000	20031203
US 20060270608	A1	20061130	US 2005-537439	20050616
MX 2005006730	A	20050908	MX 2005-6730	20050617
NO 2005003464	A	20050826	NO 2005-3464	20050715
ZA 2005004657	A	20060329	ZA 2005-4657	20060116
PRIORITY APPLN. INFO.:			IT 2002-MI2658 A	20021217
			WO 2003-EP50932 W	20031203
OTHER SOURCE(S):	MARPAT 141:71285			

GI



I



II

AB The invention relates to a preparation of nitrooxy derivs. of formula R-NR1-(K)0-1-(B)0-1-(C)0-1-NO2 [wherein: R is a radical of analgesic drug for chronic pain, for instance neurophatic pain; R1 is H or C1-5alkyl; K is C(O) or a bivalent radical, etc.; B is such that its precursor is selected from amino acids, hydroxy acids, polyalc., etc.; C is a bivalent radical containing aliphatic, heterocyclic, or aromatic radical, etc.], useful as drugs for chronic pain. Prepared compds. were screened for analgesic activity in writhing test, paw licking test, and animal model of neuropathic pain. For instance, nitrooxy derivative I (writhing test: dose - 3 mg/kg; I - 15 contractions, gabapentin - 22 contractions) was prepared via esterification of 4-(chloromethyl)benzoyl chloride by N-hydroxysuccinimide, amidation of the obtained ester II by 2-(aminomethyl)-2-cyclohexanylacetic acid, and subsequent nitration by AgNO3 (example 1).

IC ICM C07C235-42
ICS C07C235-12; C07C271-22; C07C271-54; A61K031-325; A61K031-16; A61P029-00

CC 23-16 (Aliphatic Compounds)
Section cross-reference(s): 1, 63

ST nitrooxy cyclohexyl acetate prepn chronic pain analgesic

IT Pain
(chronic, treatment of; preparation of nitrooxy-derivs. of cyclohexaneacetic acid useful as drugs for chronic pain)

IT Analgesics
(preparation of nitrooxy-derivs. of cyclohexaneacetic acid useful as drugs for chronic pain)

IT 50-78-2, Aspirin 69-72-7, Salicylic acid, biological studies 103-90-2, Paracetamol 5104-49-4, Flurbiprofen 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 22204-53-1, Naproxen
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(drug containing radical of; preparation of nitrooxy-derivs. of cyclohexaneacetic acid useful as drugs for chronic pain)

IT 713123-22-9P 713123-24-1P 713123-26-3P 713123-28-5P 713123-30-9P 713123-31-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of nitrooxy-derivs. of cyclohexaneacetic acid useful as drugs for chronic pain)

IT 713123-20-7P 713123-25-2P 713123-27-4P 713123-29-6P 713123-32-1P 713123-33-2P 713123-34-3P 713123-35-4P 713123-36-5P 713123-37-6P 713123-38-7P 713123-39-8P 713123-40-1P 713123-41-2P 713123-42-3P 713123-43-4P 713123-44-5P 713123-45-6P 713123-46-7P 713123-47-8P 713123-48-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of nitrooxy-derivs. of cyclohexaneacetic acid useful as drugs for chronic pain)
IT 60142-96-3, Gabapentin
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant and comparative compound; preparation of nitrooxy-derivs. of cyclohexaneacetic acid useful as drugs for chronic pain)
IT 876-08-4 6066-82-6 7761-88-8, Silver nitrate, reactions 22128-62-7, Chloromethyl chloroformate 37693-18-8, 4-Chlorobutyl chloroformate 74597-04-9, 3-Bromomethylphenol
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of nitrooxy-derivs. of cyclohexaneacetic acid useful as drugs for chronic pain)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 11 OF 32 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:454462 ZCAPLUS Full-text
DOCUMENT NUMBER: 141:33709
TITLE: Cooperation between aspirin-triggered lipoxin and nitric oxide (NO) mediates antiadhesive properties of 2-(acetyloxy)benzoic acid 3-(nitrooxymethyl)phenyl ester (NCX-4016) (NO-aspirin) on neutrophil-endothelial cell adherence
AUTHOR(S): Fiorucci, Stefano; Distrutti, Eleonora; Mencarelli, Andrea; Rizzo, Giovanni; Di Lorenzo, Anna Rita; Baldoni, Monia; Del Soldato, Piero; Morelli, Antonio; Wallace, John L.
CORPORATE SOURCE: Clinica di Gastroenterologia ed Epatologia, Dipartimento di Medicina Clinica e Sperimentale, Universita degli Studi di Perugia, Perugia, Italy
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2004), 309(3), 1174-1182
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 2-(Acetyloxy)benzoic acid 3-(nitrooxymethyl)phenyl ester (NCX-4016) is a nitric oxide (NO)-releasing derivative of aspirin that inhibits cyclooxygenase (COX) activity and releases NO. Acetylation of COX-2 by aspirin activates a transcellular biosynthetic pathway that switches eicosanoid biosynthesis from prostaglandin E2 to 15-epi-lipoxin (LX)A4 or aspirin-triggered lipoxin (ATL). Here, we demonstrate that exposure of neutrophil (PMN)/human umbilical vein endothelial cell (HUVEC) cocultures to aspirin and NCX-4016 triggers ATL formation and inhibits cell-to-cell adhesion induced by endotoxin (LPS) and interleukin (IL)-1β by 70 to 90%. However, although selective and nonselective COX-2 inhibitors (celecoxib, rofecoxib, and naproxen) or N-tert-butoxycarbonyl-methionine-leucine-phenylalanine (Boc-1), an LXA4 receptor antagonist, reduced the antiadhesive properties of aspirin by ≈70%, antiadhesive effects of NCX-4016 were only marginally affected (≈30%) by COX inhibitors and Boc-1, implying that COX-independent mechanisms mediate the antiadhesive properties of NCX-4016. Indeed, NCX-4016 causes a long-lasting (up to 12 h) release of NO and cGMP accumulation in HUVEC. Scavenging NO with 10 mM Hb, in the presence of celecoxib, reduced the antiadhesive properties of NCX-4016 by ≈80%. Confirming a role for NO, the NO donor diethylenetriamine-NO also inhibited PMN/HUVEC adhesion by ≈80%. NCX-4016, but not aspirin, decreased DNA binding of nuclear factor-κB (NF-κB) on gel shift anal. and

HUVEC's overexpression of CD54 and CD62E induced by LPS/IL-1β. Reduction of binding of the two NF-κB subunits p50-p50 and p50-p65 was reversed by dithiothreitol, implying S-nitrosylation as mechanism of inhibition. In summary, our results support that ATL and NO are formed at the PMN/HUVEC interface after exposure to NCX-4016 and mediate the antiadhesive properties of this compound

CC 1-12 (Pharmacology)

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 12 OF 32 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:368290 ZCAPLUS Full-text

DOCUMENT NUMBER: 140:417559

TITLE: Gastric tolerability and prolonged prostaglandin inhibition in the brain with a nitric oxide-releasing flurbiprofen derivative, NCX-2216 [3-[4-(2-fluoro-α-methyl-[1,1'-biphenyl]-4-acetyloxy)-3-methoxyphenyl]-2-propenoic acid 4-nitrooxy butyl ester]

AUTHOR(S): Wallace, John L.; Muscara, Marcelo N.; De Nucci, Gilberto; Zamuner, Stella; Cirino, Giuseppe; Del Soldato, Piero; Ongini, Ennio

CORPORATE SOURCE: Department of Pharmacology and Therapeutics, University of Calgary, Calgary, AB, Can.

SOURCE: Journal of Pharmacology and Experimental Therapeutics (2004), 309(2), 626-633
CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB NCX-2216 [3-[4-(2-fluoro-α-methyl-[1,1'-biphenyl]-4-acetyloxy)-3-methoxyphenyl]-2-propenoic acid 4-nitrooxy Bu ester] is an NO-releasing flurbiprofen derivative that also contains a ferulic acid (antioxidant) moiety. NCX-2216 has been shown to be effective in reducing β-amyloid deposition in a transgenic mouse model of Alzheimer's disease. The tolerability of this compound in the stomach and its ability to suppress prostaglandin synthesis in the brain are not known. The purpose of this study was to assess the contribution of nitric oxide (NO) and ferulic acid to the pharmacol. properties of NCX-2216 vs. flurbiprofen; thus, we compared their gastric tolerability and suppression of prostaglandin synthesis, peripherally and centrally. Oral flurbiprofen produced extensive gastric damage and suppressed gastric prostaglandin synthesis. In contrast, while suppressing prostaglandin production, equimolar doses of NCX-2216 did not cause detectable gastric injury. The NO-releasing moiety of NCX-2216 (but not the ferulic acid moiety) was crucial for the gastric safety of this compound NCX-2216 substantially inhibited prostanoid synthesis despite not being detectable in plasma and despite producing only low amts. of flurbiprofen in plasma and in the brain. Inhibition of brain prostaglandin synthesis by NCX-2216 (22 mg/kg) persisted for a much longer period of time (up to 48 h) than was seen with flurbiprofen (≤12 h). These results demonstrate that a single administration of NCX-2216 can produce prolonged suppression of brain prostaglandin synthesis without causing gastric injury. It is likely that an active metabolite of NCX-2216 contributes to the suppression of cyclooxygenase activity. NCX-2216 may represent an attractive alternative to conventional nonsteroidal anti-inflammatory drugs for long-term treatment of a variety of inflammatory disorders, especially those occurring in the central nervous system.

CC 1-7 (Pharmacology)

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 13 OF 32 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:203792 ZCAPLUS Full-text
DOCUMENT NUMBER: 140:253345
TITLE: Process for preparing nitrooxyalkyl esters of carboxylic acids
INVENTOR(S): Del Soldato, Piero; Santus, Giancarlo; Benedini, Francesca
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004020385	A1	20040311	WO 2003-EP8700	20030806
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003266261	A1	20040319	AU 2003-266261	20030806
EP 1537070	A1	20050608	EP 2003-790866	20030806
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1678560	A	20051005	CN 2003-820605	20030806
CN 1326830	C	20070718		
JP 2005536559	T	20051202	JP 2004-532055	20030806
ZA 2005000890	A	20060222	ZA 2005-890	20050131
US 20070112194	A1	20070517	US 2006-522986	20060913
PRIORITY APPLN. INFO.:			IT 2002-MI1861 A	20020829
			WO 2003-EP8700 W	20030806

OTHER SOURCE(S): CASREACT 140:253345; MARPAT 140:253345

AB RCO2(CR1R2)m(CR3R4)n(CR5R6)oXp(CR7R8)q(CR9R10)r(CR11R12)sONO2 [R = residue of a pharmaceutically active compound, ferulic acid; R1-R12 = H, alkyl, aralkyl; m, n, o, q, r, s = 0-6; p = 0, 1; X = O, S, SO, SO2, NR13, PR13, (substituted) cycloalkylene, arylene, heterocyclylene; R13 = H, alkyl], were prepared by reaction of RCO2Z (R as defined above; Z = H, Li+, Na+, K+, Ca++, Mg++, tetralkylammonium, tetralkylphosphonium) with Y(CR1R2)m(CR3R4)n(CR5R6)oXp(CR7R8)q(CR9R10)r(CR11R12)sONO2 [Y = Br, Cl, iodo, BF4, SbF6, FSO3, ASO3; A = (substituted) alkyl; other variables as defined above]. Thus, ferulic acid, 4-nitrooxybutyl bromide, and Et3N were stirred 3 days in DMF to give 65% ferulic acid 4-nitrooxybutyl ester.

IC ICM C07C203-04
ICS C07C201-02

CC 25-18 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)

ST nitrooxyalkyl ester carboxylic acid prepn; ferulic acid nitrooxybutyl ester prepn

IT Esterification
(preparation of nitrooxyalkyl esters of carboxylic acids)

IT 257626-10-1P, 5-tert-Butoxycarbonylamino-2-hydroxybenzoic acid 4-

nitrooxybutyl ester 475561-36-5P,
(E)-3-(4-Hydroxy-3-methoxyphenyl)-2-propenoic acid 4-nitrooxybutyl ester
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of nitrooxyalkyl esters of carboxylic acids)
IT 67-56-1, Methanol, uses 68-12-2, Dmf, uses
RL: NUU (Other use, unclassified); USES (Uses)
(preparation of nitrooxyalkyl esters of carboxylic acids)
IT 98-59-9, Tosyl chloride 1135-24-6, Ferulic acid 33036-62-3, 4-Bromobutanol 135321-95-8, 5-tert-Butoxycarbonylaminosalicylic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of nitrooxyalkyl esters of carboxylic acids)
IT 146563-40-8P, 4-Nitrooxybutyl bromide 151109-66-9P, (E)-3-(4-Hydroxy-3-methoxyphenyl)-2-propenoic acid potassium salt 669692-75-5P, 4-Nitrooxybutyl p-toluenesulfonate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of nitrooxyalkyl esters of carboxylic acids)
IT 110-86-1, Pyridine, reactions 121-44-8, Triethylamine, reactions 1310-58-3, Potassium hydroxide, reactions 7664-93-9, Sulfuric acid, reactions 7697-37-2, Nitric acid, reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(preparation of nitrooxyalkyl esters of carboxylic acids)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 14 OF 32 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:203791 ZCAPLUS Full-text
DOCUMENT NUMBER: 140:253349
TITLE: Process for preparing nitrooxyalkyl esters of naproxen and bromonaproxen.
INVENTOR(S): Del Soldato, Piero; Santus, Giancarlo; Benedini, Francesca
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004020384	A1	20040311	WO 2003-EP8698	20030806
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2497187	A1	20040311	CA 2003-2497187	20030806
AU 2003266966	A1	20040319	AU 2003-266966	20030806
EP 1532098	A1	20050525	EP 2003-747879	20030806
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

CN 1678560	A	20051005	CN 2003-820605		20030806
CN 1326830	C	20070718			
JP 2005536558	T	20051202	JP 2004-532054		20030806
NZ 537993	A	20061130	NZ 2003-537993		20030806
RU 2315035	C2	20080120	RU 2005-104419		20030806
ZA 2005000890	A	20060222	ZA 2005-890		20050131
IN 2005CN00332	A	20070824	IN 2005-CN332		20050328
US 2006017305	A1	20060803	US 2005-523722		20050914
US 7199258	B2	20070403			
PRIORITY APPLN. INFO.:			IT 2002-MI1861	A	20020829
			WO 2003-EP8698	W	20030806

OTHER SOURCE(S): CASREACT 140:253349; MARPAT 140:253349

AB RCO2(CR1R2)m(CR3R4)n(CR5R6)oXp(CR7R8)q(CR9R10)r(CR11R12)sONO2 [R = naproxen, bromonaproxen residue; R1-R12 = H, alkyl, aralkyl; m, n, o, q, r, s = 0-6; p = 0, 1; X = O, S, SO, SO2, NR13, PR13, (substituted) cycloalkylene, arylene, heterocyclylene; R13 = H, alkyl], were prepared by reaction of RCO2Z (R as defined above; Z = H, Li+, Na+, K+, Ca++, Mg++, tetralkylammonium, tetralkylphosphonium) with Y(CR1R2)m(CR3R4)n(CR5R6)oXp(CR7R8)q(CR9R10)r(CR11R12)sONO2 [Y = halo, BF4, SbF6, FSO3, ASO3; A = (substituted) alkyl; other variables as defined above]. Thus, a mixture of naproxen and KHCO3 was heated in DMF at 50-60° for 90 min.; the mixture was cooled to room temperature and treated with KI and 4-bromobutyl nitrate (preparation given) followed by stirring for 25 h to give 73% naproxen 4-nitrooxybutyl ester.

IC ICM C07C201-02
ICS C07C203-04

CC 25-24 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)

ST nitrooxyalkyl ester naproxen bromonaproxen prepn; methoxynaphthylpropionic acid bromobutyl nitrate esterification reaction

IT Esterification
(preparation of nitrooxyalkyl esters of naproxen and bromonaproxen)

IT 14797-55-8P, Nitrate, preparation
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(esters; preparation of nitrooxyalkyl esters of naproxen and bromonaproxen)

IT 163133-43-5P, (S)-2-(6-Methoxy-2-naphthyl)propanoic acid 4-nitrooxybutyl ester 669692-80-2P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of nitrooxyalkyl esters of naproxen and bromonaproxen)

IT 68-12-2, Dmf, uses
RL: NUU (Other use, unclassified); USES (Uses)
(preparation of nitrooxyalkyl esters of naproxen and bromonaproxen)

IT 98-59-9, Tosyl chloride 22204-53-1, Naproxen 33036-62-3, 4-Bromobutanol 84236-26-0, (S)-2-(5-Bromo-6-methoxy-2-naphthyl)propanoic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of nitrooxyalkyl esters of naproxen and bromonaproxen)

IT 110798-26-0P, 4-Bromobutyl tosylate 146563-40-8P, 4-Bromobutyl nitrate 669692-75-5P, 4-Nitrooxybutyl p-toluenesulfonate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of nitrooxyalkyl esters of naproxen and bromonaproxen)

IT 110-86-1, Pyridine, reactions 121-44-8, Triethylamine, reactions

298-14-6, Potassium bicarbonate 7664-93-9, Sulfuric acid, reactions 7681-11-0, Potassium iodide, reactions 7697-37-2, Nitric acid, reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(preparation of nitrooxyalkyl esters of naproxen and bromonaproxen)
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 15 OF 32 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:2830 ZCAPLUS Full-text
DOCUMENT NUMBER: 140:59410
TITLE: Preparation of nitrooxy derivatives of cyclooxygenase-2 inhibitors
INVENTOR(S): Del Soldato, Piero; Santus, Giancarlo
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000781	A2	20031231	WO 2003-EP6502	20030620
WO 2004000781	A3	20041014		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IT 2002MI1391	A1	20031229	IT 2002-MI1391	20020625
CA 2491209	A1	20031231	CA 2003-2491209	20030620
AU 2003245972	A1	20040106	AU 2003-245972	20030620
EP 1517889	A2	20050330	EP 2003-738069	20030620
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1662490	A	20050831	CN 2003-814682	20030620
JP 2005530836	T	20051013	JP 2004-514803	20030620
NZ 537043	A	20060929	NZ 2003-537043	20030620
RU 2339617	C2	20081127	RU 2004-138552	20030620
ZA 2004010060	A	20051020	ZA 2004-10060	20041213
MX 2004012851	A	20050224	MX 2004-12851	20041216
US 20060106082	A1	20060518	US 2005-516938	20050913
PRIORITY APPLN. INFO.:			IT 2002-MI1391 A	20020625
			WO 2003-EP6502 W	20030620

OTHER SOURCE(S): MARPAT 140:59410
AB Disclosed are new compds. able to release COX-2 inhibitors and NO (no data) having formula M-T-YA-NO2 [wherein M-T = the residue of a COX-2 selective inhibitor (T = SO2NH, SO2NR, CO, O, S, NH, N(SO2R); R = C1-10 alkyl; the COX-2 selective inhibitor, M-TH or M-TOH, has to meet test 2 mentioned in the description); YA = -(B)b0-(C)c0- [b0, c0 = 0,1, with the proviso that b0 and c0 cannot be simultaneously 0; B = TB-X2-TB1; TB = CO, X; X = O, S, NH, NR, R (defined above); TB = CO when T = SO2NH, SO2NR-O, S, NH, or N(SO2R), TB = X when T = CO; TB1 = CO or X (defined above); X2 = a divalent radical selected

from the following compds. Q or Q1, etc. (n1, n2 = 0, 1; R2, R3 = H, Me; Y1 = CH2CH2, CH:CH(CH2)n2; n2 = 0, 1)]] for the treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, Alzheimer's disease, or disorders resulting from elevated levels of COX-2. These compds. including 5-niroxypentanoc acid, 4-nitrooxybutyric acid, and 4-nitrooxybutyramide, 2-nitroxymethylbenzoic acid ester derivs. mitigate or remove the known side-effects of COX-2 inhibitors. The inflammatory disorders are selected from the group consisting of, but not limited to, arthritis, rheumatoid arthritis, osteoarthritis, allergic rhinitis, sinusitis, chronic obstructive pulmonary diseases, dermatitis, psoriasis, cystic fibrosis, multiple sclerosis, vasculitis and organ transplant rejection. The cardiovascular diseases are selected from the group consisting of, but not limited to, atherosclerosis, restenosis, coronary artery disease, angina, diabetes mellitus, diabetic nephropathy, diabetic retinopathy, stroke and myocardial infarct. The gastrointestinal disorders are selected from the group consisting of, but not limited to, inflammatory intestinal disorders, Crohn's disease, gastritis, ulcerative colitis, peptic ulcer, hemorrhagic ulcer, gastric hyperacidity, dyspepsia, gastroparesis, Zollinger-Ellison's syndrome, bacterial infections, hypersecretory states associated with systemic mastocytosis or basophilic leukemia and hyperhystaminemia. The disorders resulting from elevated levels of COX-2 are selected from the group consisting of, but not limited to, angiogenesis, arthritis, asthma, bronchitis, menstrual cramps, tendonitis, bursitis, neoplasia, ophthalmic diseases, pulmonary inflammations, central nervous system disorders, allergic rhinitis, atherosclerosis, endothelial disorders, organs and tissues preservation, inhibition and/or prevention of platelets aggregation. Thus, N-[6-[(2,4-difluorophenyl)thio]-2,3-dihydro-1-oxo-1-inden-5-yl]-N-[4- (chloro)butyroyloxymethyl]methanesulfonamide. A solution of chloromethyl (4-chloro)butyrate (1 g, 5.40 mmol) in anhydrous THF (5 mL) was slowly added dropwise in a suspension of N-[6-[(2,4-difluorophenyl)thio]-2,3-dihydro-1- oxo-1-inden-5-yl]methanesulfonamide sodium salt (2.04 g, 5.40 mmol) in anhydrous THF (25 mL) and stirred at room temperature overnight to give, after workup and silica gel chromatog., N-[6-[(2,4-difluorophenyl)thio]-2,3-dihydro-1-oxo-1-inden-5-yl]-N-[4-(chloro)butyroyloxymethyl]methanesulfonamide (I). A solution of I (1 g, 1.98 mmol) in MeCN (20 mL) was added with AgNO3 (0.67 g, 3.96 mmol), heated at 80° for 15 h in the absence of light, filtered to remove the silver salt, evaporated under vacuum, and purified by chromatog. on a silica gel column to give with n-hexane/ethyl acetate 8/2 as eluent to give 503 mg N-[6-[(2,4-difluorophenyl)thio]-2,3-dihydro-1-oxo-1-inden-5-yl]-N-[4-(nitrooxy)butyroyloxymethyl]methanesulfonamide.

IC ICM C07C203-04

CC 25-19 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1, 7

ST nitrooxy deriv cyclooxygenase 2 inhibitor prepn; nitrooxybutyric acid prepn prodrug cyclooxygenase 2 inhibitor; niroxypentanoc acid prepn prodrug cyclooxygenase 2 inhibitor; nitrooxybutyramide prepn prodrug cyclooxygenase 2 inhibitor; nitroxymethylbenzoic acid ester prepn prodrug cyclooxygenase 2 inhibitor; inflammatory disorder prevention treatment nitrooxy deriv COX2 inhibitor prepn; pain fever prevention treatment nitrooxy deriv COX2 inhibitor prepn; cardiovascular disease prevention treatment nitrooxy deriv COX2 inhibitor prepn; gastrointestinal disorder prevention treatment nitrooxy deriv COX2 inhibitor prepn; tumor prevention treatment nitrooxy deriv COX2 inhibitor prepn; Alzheimer disease prevention treatment nitrooxy deriv COX2 inhibitor prepn

IT Inflammation
(Crohn's disease; preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease,

gastrointestinal disorders, tumors, or Alzheimer's disease)
IT Intestine, disease
(Crohn's; preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)
IT Pancreas, neoplasm
(Zollinger-Ellison syndrome; preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)
IT Allergy
Inflammation
Nose, disease
(allergic rhinitis; preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)
IT Heart, disease
(angina pectoris; preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)
IT Antiarteriosclerotics
(antiatherosclerotics; preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)
IT Infection
(bacterial; preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)
IT Bronchi, disease
Inflammation
(bronchitis; preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)
IT Joint, anatomical
(bursa, bursitis (inflammation); preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)
IT Lung, disease
(chronic obstructive pulmonary disease; preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)
IT Artery, disease
(coronary; preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)
IT Kidney, disease
(diabetic nephropathy; preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)
IT Eye, disease

(diabetic retinopathy; preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)

IT Tendon
(disease, tendinitis, endothelial diseases; preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)

IT Tendon
(disease, tendinitis; preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)

IT Inflammation
Stomach, disease
(gastritis; preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)

IT Stomach, disease
(gastroparesis; preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)

IT Ulcer
(hemorrhagic; preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)

IT Gastric acid
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hyperacidity; preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)

IT Heart, disease
(infarction; preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)

IT Intestine, disease
(inflammatory; preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)

IT Ulcer
(peptic; preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)

IT Inflammation
Lung, disease
(pneumonitis; preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)

IT Alzheimer's disease
Analgesics
Angiogenesis

Angiogenesis inhibitors
Anti-Alzheimer's agents
Anti-inflammatory agents
Antiarthritics
Antiasthmatics
Antibacterial agents
Antidiabetic agents
Antipyretics
Antitumor agents
Antiulcer agents
Arthritis
Asthma
Atherosclerosis
Cardiovascular agents
Cardiovascular system, disease
Central nervous system, disease
Cystic fibrosis
Dermatitis
Diabetes mellitus
Digestive tract, disease
Dyspepsia
Eye, disease
Fever and Hyperthermia
Inflammation
Multiple sclerosis
Neoplasm
Nervous system agents
Osteoarthritis
Pain
Platelet aggregation inhibitors
Psoriasis
Rheumatoid arthritis
(preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)

IT Drug delivery systems
(prodrugs; preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)

IT Transplant and Transplantation
(rejection inhibitors; preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)

IT Artery, disease
(restenosis; preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)

IT Inflammation
Respiratory system, disease
(sinusitis; preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)

IT Muscle, disease
(spasm, menstrual; preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of

inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)

IT Brain, disease
(stroke; preparation of nitrooxy derivs. of cyclooxygenase -2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)

IT Inflammation
(tendinitis, endothelial diseases; preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)

IT Inflammation
(tendinitis; preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)

IT Digestive tract, disease
(ulcer, peptic; preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)

IT Inflammation
Intestine, disease
(ulcerative colitis; preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)

IT Blood vessel, disease
Inflammation
(vasculitis; preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)

IT 179174-76-6P 637779-31-8P 637779-32-9P 637779-33-0P 637779-34-1P 637779-36-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)

IT 220991-20-8P, 2-[(2-Chloro-6-fluorophenyl)amino]-5-methylbenzeneacetic acid 586347-45-7P 637779-24-9P 637779-25-0P 637779-26-1P 637779-27-2P 637779-29-4P, N-(4-Nitro-2-cyclohexyloxyphenyl)methanesulfonanilide 637779-30-7P, 2-[(2-Chloro-6-fluorophenyl)amino]-4-methylbenzeneacetic acid
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)

IT 329900-75-6, Cyclooxygenase-2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prodrugs releasing cyclooxygenase-2 inhibitors and NO; preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors)

IT 876-08-4, 4-Chloromethylbenzoyl chloride 4635-59-0, 4-Chlorobutyryl

chloride 7761-88-8, Silver nitrate, reactions 80418-49-1
161639-92-5, N-(2-Phenoxy-4-nitrophenyl)methanesulfonamide sodium salt
162011-90-7, 3-[Phenyl-4-(4-methylsulfonyl)phenyl]-2(5H)-furanone
251295-68-8, Chloromethyl 3-(chloromethyl)benzoate 467427-58-3,
N-[6-[(2,4-Difluorophenyl)thio]-2,3-dihydro-1-oxo-1-inden-5-
yl]methanesulfonamide sodium salt 637779-35-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of nitrooxy derivs. of
cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of
inflammatory disorders, pain, fever, cardiovascular disease,
gastrointestinal disorders, tumors, or Alzheimer's disease)
IT 10102-43-9, Nitrogen monoxide, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(release; preparation of nitrooxy derivs. of
cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of
inflammatory disorders, pain, fever, cardiovascular disease,
gastrointestinal disorders, tumors, or Alzheimer's disease)
IT 158205-05-1P, N-[6-[(2,4-Difluorophenyl)thio]-2,3-dihydro-1-oxo-1H-inden-5-
yl]methanesulfonamide 169590-42-5P,
4-[5-(4-Methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-
yl]benzenesulfonamide 180200-68-4P,
4-(4-Cyclohexyl-2-methyloxazol-5-yl)-2-fluorobenzenesulfonamide
637779-28-3P, N-(4-Nitro-2-phenoxyphenyl)methanesulfonanilide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(selective cyclooxygenase-2 inhibitor, prodrugs for; preparation
of nitrooxy derivs. of cyclooxygenase-2 inhibitors)
IT 181695-72-7, 4-(5-Methyl-3-phenylisoxazol-4-yl)benzenesulfonamide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(selective cyclooxygenase-2 inhibitor, prodrugs for; preparation
of nitrooxy derivs. of cyclooxygenase-2 inhibitors)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 16 OF 32 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:2684 ZCAPLUS Full-text
DOCUMENT NUMBER: 140:73178
TITLE: Nitroxy derivatives of non-steroidal anti-inflammatory
compounds as selective inhibitors of
cyclooxygenase-2 for the treatment of inflammation
INVENTOR(S): Del Soldato, Piero; Santus, Giancarlo
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000300	A1	20031231	WO 2003-EP6651	20030624
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

IT	2002MI1399	A1	20031229	IT 2002-MI1399		20020625
AU	2003238042	A1	20040106	AU 2003-238042		20030624
PRIORITY APPLN. INFO.:				IT 2002-MI1399	A	20020625
				WO 2003-EP6651	W	20030624

OTHER SOURCE(S): MARPAT 140:73178

AB The present invention relates to compds. able to inhibit selectively the enzyme cyclooxygenase-2 (COX-2) without inhibiting substantially the enzyme COX-1. Specifically, the present invention concerns nitroxy derivs. of non-steroidal anti-inflammatory compds., which are able to inhibit selectively the enzyme COX-2. The compds. of the invention are useful in the treatment and/or prophylaxis of inflammatory processes.

IC ICM A61K031-21
ICS A61K031-44; A61K031-445; A61K031-496; A61K031-621; A61P019-02; A61P025-00; A61P043-00

CC 7-3 (Enzymes)
Section cross-reference(s): 1, 63

ST cyclooxygenase 2 inhibitor drug antiinflammatory nitroxy deriv

IT Disease, animal
(COX-2 elevated level associated; nitroxy derivs. of non-steroidal anti-inflammatory compds. as selective inhibitors of cyclooxygenase-2 for treatment of inflammation)

IT Polyoxyalkylenes, biological studies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(COX-2 inhibitors containing; nitroxy derivs. of non-steroidal anti-inflammatory compds. as selective inhibitors of cyclooxygenase-2 for treatment of inflammation)

IT Functional groups
(alkylenoxy group, COX-2 inhibitors containing; nitroxy derivs. of non-steroidal anti-inflammatory compds. as selective inhibitors of cyclooxygenase-2 for treatment of inflammation)

IT Analgesics
Anti-inflammatory agents
Antiarthritics
Antipyretics
Drug targets
Drugs
Inflammation
(nitroxy derivs. of non-steroidal anti-inflammatory compds. as selective inhibitors of cyclooxygenase-2 for treatment of inflammation)

IT Arthritis
Fever and Hyperthermia
Osteoarthritis
Pain
(treatment of; nitroxy derivs. of non-steroidal anti-inflammatory compds. as selective inhibitors of cyclooxygenase-2 for treatment of inflammation)

IT 103-84-4 110-85-0D, Piperazine, derivs. 110-86-1D, Pyridine, derivs. 110-89-4D, Piperidine, derivs. 110-91-8D, Morpholine, derivs., biological studies 122-39-4D, derivs. 123-75-1D, Pyrrolidine, derivs. 134-55-4D, derivs. 142-68-7D, derivs. 288-32-4D, 1H-Imidazole, derivs. 289-80-5D, Pyridazine, derivs. 289-95-2D, Pyrimidine, derivs. 290-37-9D, Pyrazine, derivs. 504-74-5D, Imidazolidine, derivs. 504-75-6 1205-39-6D, derivs. 3337-17-5D, derivs. 6631-37-4D, derivs. 6933-26-2D, derivs. 21388-17-0 22960-94-7D, derivs. 25322-68-3,

Polyethylene glycol 25322-69-4, Polypropylene glycol 37940-57-1D, derivs. 41201-70-1D, derivs. 52779-81-4D, derivs. 55258-76-9 62128-36-3D, derivs. 66067-43-4D, derivs. 71969-36-3D, derivs. 78427-95-9D, derivs. 78967-05-2D, derivs. 92841-23-1D, derivs. 100319-40-2 115066-03-0 115967-34-5 134891-27-3 138584-29-9 639857-61-7, Poly[oxy[2-(nitrooxy)-1,3-propanediyl]] 639857-62-8D, derivs. 639857-63-9D, derivs. 639857-64-0D, derivs. 639857-65-1D, derivs. 639857-66-2D, derivs. 639857-67-3 639857-68-4 639857-69-5 639857-71-9 639857-72-0 639857-73-1 639857-74-2 640249-19-0, Poly[oxy[(nitrooxy)-1,3-propanediyl]]
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(COX-2 inhibitors containing; nitroxy derivs. of non-steroidal anti-inflammatory compds. as selective inhibitors of cyclooxygenase-2 for treatment of inflammation)

IT 329900-75-6, Cyclooxygenase-2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(nitroxy derivs. of non-steroidal anti-inflammatory compds. as selective inhibitors of cyclooxygenase-2 for treatment of inflammation)

IT 290335-35-2 302543-75-5 302543-76-6 302543-77-7 302543-78-8 302543-79-9 410071-14-6 475561-43-4 497818-54-9 612478-31-6 639857-75-3 639857-76-4 639857-77-5 639857-78-6 639857-79-7 639857-80-0 639857-81-1 639857-82-2 639857-83-3 639858-04-1
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nitroxy derivs. of non-steroidal anti-inflammatory compds. as selective inhibitors of cyclooxygenase-2 for treatment of inflammation)

IT 109-64-8, 1,3-Dibromopropane 26159-34-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of methoxymethylnaphthalenacetic acid bromopropyl ester; nitroxy derivs. of non-steroidal anti-inflammatory compds. as selective inhibitors of cyclooxygenase-2 for treatment of inflammation)

IT 34782-06-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of methoxymethylnaphthalenacetic acid chloropropylpiperazinylpropyl ester; nitroxy derivs. of non-steroidal anti-inflammatory compds. as selective inhibitors of cyclooxygenase-2 for treatment of inflammation)

IT 639857-84-4P 639857-85-5P 639857-86-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of methoxymethylnaphthalenacetic acid nitrooxypropylpiperazinylpropyl ester dihydrochloride; nitroxy derivs. of non-steroidal anti-inflammatory compds. as selective inhibitors of cyclooxygenase-2 for treatment of inflammation)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

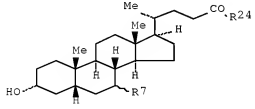
L31 ANSWER 17 OF 32 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:913178 ZCAPLUS Full-text
DOCUMENT NUMBER: 139:381668
TITLE: Preparation of ursodeoxycholic acid nitrooxy esters for use in pharmaceutical compositions for the treatment of acute dysfunction of portal and hepatic venous circulation
INVENTOR(S): Del Soldato, Piero; Acuto, Giancarlo
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 31 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003095471	A2	20031120	WO 2003-EP4861	20030509
WO 2003095471	A3	20040401		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IT 2002MI1025	A1	20031114	IT 2002-MI1025	20020514
AU 2003224154	A1	20031111	AU 2003-224154	20030509
CA 2485146	A1	20031120	CA 2003-2485146	20030509
EP 1504020	A2	20050209	EP 2003-720562	20030509
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1653083	A	20050810	CN 2003-810211	20030509
CN 100347186	C	20071107		
JP 2005526127	T	20050902	JP 2004-503485	20030509
NZ 535740	A	20061027	NZ 2003-535740	20030509
RU 2299886	C2	20070527	RU 2004-132864	20030509
ZA 2004007911	A	20050701	ZA 2004-7911	20040930
MX 2004011233	A	20050125	MX 2004-11233	20041112
NO 2004005437	A	20041213	NO 2004-5437	20041213
US 20060094664	A1	20060504	US 2005-512856	20050519

PRIORITY APPLN. INFO.: IT 2002-MI1025 A 20020514
WO 2003-EP4861 W 20030509

OTHER SOURCE(S): MARPAT 139:381668
GI



I

AB Ursodeoxycholic acid derivs., such as I [R7 = α-, β-OH; R24 = (B)m-(C)n-ONO2; B = ester linking group derived from compds. such as ferulic acid or amide linking group derived from compds. such as histidine; C = ester linking group such as alkylene or cycloalkene; m, n = 0, 1], were prepared for therapeutic use in the treatment of acute dysfunction of portal and hepatic venous circulation. Thus, (3α,5β,7β)-3,7-dihydroxycholan-24-oic acid 4-

(nitrooxy)butyl ester I [R7 = β-OH, R24 = O(CH2)4ONO2] was prepared by an esterification reaction of ursodeoxycholic acid with 1,4-dibromobutane using NaOAc in DMF and subsequent treatment of the intermediate bromobutyl ester I [R7 = β-OH, R24 = O(CH2)4Br] with AgNO3 in MeCN. The effects of ursodeoxycholic acid and ester II were tested in an exptl. model of hepatic and portal venous circulation disorder in rats induced by ligature of the biliary duct and subsequent treatment with norepinephrine.

IC ICM C07J041-00
ICS A61K031-575; A61K031-58; A61P001-16

CC 32-6 (Steroids)
Section cross-reference(s): 1, 63

ST ursodeoxycholate nitrooxy deriv prepn portal hepatic venous circulation; liver disease treatment ursodeoxycholate nitrooxy deriv prepn

IT Liver, disease
(treatment; preparation of ursodeoxycholic acid nitrooxy esters for use in pharmaceutical compns. for the treatment of acute dysfunction of portal and hepatic venous circulation)

IT Circulation
(venous, portal and hepatic; preparation of ursodeoxycholic acid nitrooxy esters for use in pharmaceutical compns. for the treatment of acute dysfunction of portal and hepatic venous circulation)

IT 50-81-7DP, Ascorbic acid, derivs. containing ursodeoxycholic acid esters 52-67-5DP, Penicillamine, derivs. containing ursodeoxycholic acid esters 52-90-4DP, L-Cysteine, derivs. containing ursodeoxycholic acid esters 56-84-8DP, L-Aspartic acid, derivs. containing ursodeoxycholic acid esters 57-50-1DP, Saccharose, derivs. containing ursodeoxycholic acid esters 60-24-2DP, 2-Mercaptoethanol, derivs. containing ursodeoxycholic acid esters 70-18-8DP, Glutathione, derivs. containing ursodeoxycholic acid esters 71-00-1DP, L-Histidine, derivs. containing ursodeoxycholic acid esters 77-92-9DP, Citric acid, derivs. containing ursodeoxycholic acid esters 80-72-8DP, Reductic acid, derivs. containing ursodeoxycholic acid esters 89-65-6DP, Isoascorbic acid, derivs. containing ursodeoxycholic acid esters 117-39-5DP, Quercetin, derivs. containing ursodeoxycholic acid esters 120-05-8DP, Sulfuretin, derivs. containing ursodeoxycholic acid esters 121-34-6DP, Vanillic acid, derivs. containing ursodeoxycholic acid esters 121-79-9DP, Propyl gallate, derivs. containing ursodeoxycholic acid esters 123-31-9DP, Hydroquinone, derivs. containing ursodeoxycholic acid esters 141-90-2DP, 2-Thiouracil, derivs. containing ursodeoxycholic acid esters 149-91-7DP, Gallic acid, derivs. containing ursodeoxycholic acid esters 154-23-4DP, Catechin, derivs. containing ursodeoxycholic acid esters 288-13-1DP, Pyrazole, derivs. containing ursodeoxycholic acid esters 303-45-7DP, Gossypol, derivs. containing ursodeoxycholic acid esters 305-84-0DP, L-Carnosine, derivs. containing ursodeoxycholic acid esters 331-39-5DP, Caffeic acid, derivs. containing ursodeoxycholic acid esters 458-35-5DP, Coniferyl alcohol, derivs. containing ursodeoxycholic acid esters 490-79-9DP, Gentisic acid, derivs. containing ursodeoxycholic acid esters 500-38-9DP, Nordihydroguaiaretic acid, derivs. containing ursodeoxycholic acid esters 501-94-0DP, derivs. containing ursodeoxycholic acid esters 520-18-3DP, Kaempferol, derivs. containing ursodeoxycholic acid esters 526-84-1DP, Dihydroxymaleic acid, derivs. containing ursodeoxycholic acid esters 533-73-3DP, Hydroxyhydroquinone, derivs. containing ursodeoxycholic acid esters 584-85-0DP, Anserine, derivs. containing ursodeoxycholic acid esters 616-91-1DP, N-Acetylcysteine, derivs. containing ursodeoxycholic acid esters 824-46-4DP, Methoxyhydroquinone, derivs. containing ursodeoxycholic acid esters 1078-61-1DP, Dihydrocaffeic acid, derivs. containing ursodeoxycholic acid esters 1135-24-6DP, Ferulic acid, derivs. containing ursodeoxycholic acid esters 3211-76-5DP, L-Selenomethionine, derivs. containing ursodeoxycholic acid esters 3614-08-2DP, Selenocysteine, derivs. containing ursodeoxycholic acid esters 3690-05-9DP, p-Coumaric alcohol,

derivs. containing ursodeoxycholic acid esters 4350-09-8DP, 5-Hydroxy-L-tryptophan, derivs. containing ursodeoxycholic acid esters 7400-08-0DP, p-Coumaric acid, derivs. containing ursodeoxycholic acid esters 15537-71-0DP, N-Acetylpenicillamine, derivs. containing ursodeoxycholic acid esters 63147-28-4DP, 3,5-Di-tert-butyl-4-hydroxybenzylthioglycolate, derivs. containing ursodeoxycholic acid esters 301828-26-2P
RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed therapeutic use and preparation; preparation of ursodeoxycholic acid nitrooxy esters for use in pharmaceutical compns. for the treatment of acute dysfunction of portal and hepatic venous circulation)

IT 128-13-2, Ursodeoxycholic acid
RL: PAC (Pharmacological activity); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(preparation of ursodeoxycholic acid nitrooxy esters for use in pharmaceutical compns. for the treatment of acute dysfunction of portal and hepatic venous circulation)

IT 624743-62-0P, (3α,5β,7β)-3,7-Dihydroxycholan-24-oic acid 4-(nitrooxy)butyl ester
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of ursodeoxycholic acid nitrooxy esters for use in pharmaceutical compns. for the treatment of acute dysfunction of portal and hepatic venous circulation)

IT 110-52-1, 1,4-Dibromobutane
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of ursodeoxycholic acid nitrooxy esters for use in pharmaceutical compns. for the treatment of acute dysfunction of portal and hepatic venous circulation)

IT 624743-63-1P, (3α,5β,7β)-3,7-Dihydroxycholan-24-oic acid 4-bromobutyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of ursodeoxycholic acid nitrooxy esters for use in pharmaceutical compns. for the treatment of acute dysfunction of portal and hepatic venous circulation)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 18 OF 32 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:818296 ZCAPLUS Full-text
DOCUMENT NUMBER: 139:302040
TITLE: Nitrooxy derivatives of antiinflammatory/analgesic compounds for the treatment of arthritis
INVENTOR(S): Del Soldato, Piero
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003084550	A1	20031016	WO 2003-EP3183	20030327
W: AE, AG, AL, AU, BA, BB, BR, BZ, CA, CN, CO, CR, CU, DM, DZ, EC,				

GD, GE, HR, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, OM, PH, PL, SG, TN, TT, UA, US, UZ, VN, YU, ZA

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

IT	2002MI0773	A1	20031013	IT 2002-MI773		20020411
AU	2003224002	A1	20031020	AU 2003-224002		20030327
EP	1492543	A1	20050105	EP 2003-720377		20030327
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
JP	2005522472	T	20050728	JP 2003-581790		20030327
US	20070010458	A1	20070111	US 2006-509675		20060913
PRIORITY APPLN. INFO.:				IT 2002-MI773	A	20020411
				WO 2003-EP3183	W	20030327

OTHER SOURCE(S): MARPAT 139:302040

AB Antiinflammatory and/or antiinflammatory/analgesic compds. having the formula A(B)b0(C)c0-N(O)s [A contains radical of nonsteroidal antiinflammatory or nonsteroidal antiinflammatory/analgesic drug; B, C = bivalent linking group; s = 1, 2; b0, c0 = 0, 1 (with proviso)], and salts thereof, are disclosed for use in the treatment of arthritis.

IC ICM A61K031-616
ICS A61K031-19; A61K031-195; A61K031-165; A61K031-216; A61K031-44; A61K031-40; A61P019-02

CC 1-7 (Pharmacology)

ST antiinflammatory analgesic nitrooxy deriv arthritis treatment

IT Lymphocyte
(IL-6 and TGFβ release; nitrooxy derivs. of antiinflammatory/analgesic compds. for treatment of arthritis)

IT Monocyte
(IL-6 release; nitrooxy derivs. of antiinflammatory/analgesic compds. for treatment of arthritis)

IT Transforming growth factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(TGF-β receptor, type II; nitrooxy derivs. of antiinflammatory/analgesic compds. for treatment of arthritis)

IT Chondrocyte
(TGFβ1 production; nitrooxy derivs. of antiinflammatory/analgesic compds. for treatment of arthritis)

IT Alcohols, biological studies
Carboxylic acids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(derivs.; nitrooxy derivs. of antiinflammatory/analgesic compds. for treatment of arthritis)

IT Carboxylic acids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydroxy, derivs.; nitrooxy derivs. of antiinflammatory/analgesic compds. for treatment of arthritis)

IT Interleukin 6
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(monocyte release of; nitrooxy derivs. of antiinflammatory/analgesic compds. for treatment of arthritis)

IT Analgesics
Antiarthritics
Arthritis
Cell proliferation

Drug toxicity
Hepatotoxicity
Human
Liver
(nitrooxy derivs. of antiinflammatory/analgesic compds. for treatment of arthritis)

IT Proteoglycans, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(nitrooxy derivs. of antiinflammatory/analgesic compds. for treatment of arthritis)

IT Amino acids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nitrooxy derivs. of antiinflammatory/analgesic compds. for treatment of arthritis)

IT Anti-inflammatory agents
(nonsteroidal; nitrooxy derivs. of antiinflammatory/analgesic compds. for treatment of arthritis)

IT Drug delivery systems
(oral; nitrooxy derivs. of antiinflammatory/analgesic compds. for treatment of arthritis)

IT Drug delivery systems
(parenterals; nitrooxy derivs. of antiinflammatory/analgesic compds. for treatment of arthritis)

IT Alcohols, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyhydric, derivs.; nitrooxy derivs. of antiinflammatory/analgesic compds. for treatment of arthritis)

IT Drug delivery systems
(topical; nitrooxy derivs. of antiinflammatory/analgesic compds. for treatment of arthritis)

IT Transforming growth factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(β-, lymphocyte release of; nitrooxy derivs. of antiinflammatory/analgesic compds. for treatment of arthritis)

IT Transforming growth factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(β1-, chondrocyte production; nitrooxy derivs. of antiinflammatory/analgesic compds. for treatment of arthritis)

IT 50-78-2D, Acetylsalicylic acid, derivs. 50-81-7D, Ascorbic acid, derivs. 52-67-5D, Penicillamine, derivs. 52-90-4D, L-Cysteine, derivs. 53-86-1D, Indomethacin, derivs. 57-50-1D, Saccharose, derivs. 60-00-4D, Edetic acid, derivs. 69-72-7D, Salicylic acid, derivs. 70-18-8D, Glutathione, derivs. 77-92-9D, Citric acid, derivs. 89-65-6D, Isoascorbic acid, derivs. 103-90-2D, Paracetamol, derivs. 110-17-8D, Fumaric acid, derivs. 111-17-1D, 3,3'-Thiodipropionic acid, derivs. 117-39-5D, Quercetin, derivs. 120-05-8D, Sulphuretin, derivs. 121-34-6D, Vanillic acid, derivs. 121-79-9D, Propyl gallate, derivs. 123-31-9D, Hydroquinone, derivs. 149-91-7D, Gallic acid, derivs. 154-23-4D, Catechin, derivs. 305-84-0D, L-Carnosine, derivs. 315-30-0D, Allopurinol, derivs. 331-39-5D, Caffeic acid, derivs. 458-35-5D, Coniferyl alcohol, derivs. 490-79-9D, Gentisic acid, derivs. 500-38-9D, Nordihydroguaiaretic acid, derivs. 501-94-0D, derivs. 520-18-3D, Kempferol, derivs. 526-84-1D, Dihydroxymaleic acid, derivs. 533-73-3D, Hydroxyhydroquinone, derivs. 584-85-0D, Anserine, derivs. 616-91-1D, N-Acetylcysteine, derivs. 824-46-4D, derivs. 1078-61-1D, Dihydrocaffeic acid, derivs. 1135-24-6D, Ferulic acid, derivs. 1464-42-2D, Selenomethionine, derivs. 3411-58-3D, L-Cysteine ethyl ester, derivs. 3538-61-2D, derivs. 3614-08-2D, Selenocysteine, derivs.

3690-05-9D, p-Cumaric alcohol, derivs. 5104-49-4D, Flurbiprofen, derivs. 7400-08-0D, p-Cumaric acid, derivs. 15537-71-0D, N-Acetylpenicillamine, derivs. 15687-27-1D, Ibuprofen, derivs. 21611-48-3D, derivs. 22071-15-4D, Ketoprofen, derivs. 26171-23-3D, Tolmetin, derivs. 31842-01-0D, Indoprofen, derivs. 33005-95-7D, Tiaprofenic acid, derivs. 36211-20-8D, Penicillamine ethyl ester, derivs. 36322-90-4D, Piroxicam, derivs. 36330-85-5D, Fenbufen, derivs. 38194-50-2D, Sulindac, derivs. 38677-85-9D, Flunixin, derivs. 41340-25-4D, Etodolac, derivs. 42924-53-8D, Nabumetone, derivs. 52549-17-4D, Pranoprofen, derivs. 53716-49-7D, Carprofen, derivs. 59587-09-6D, N-Acetylcysteine ethyl ester, derivs. 59804-37-4D, Tenoxicam, derivs. 60654-26-4D, L-Cysteine propyl ester, derivs. 63147-28-4D, 3,5-Di-tert-butyl-4-hydroxybenzylthioglycolate, derivs. 67607-91-4D, derivs. 68767-14-6D, Loxoprofen, derivs. 69956-77-0D, derivs. 70374-39-9D, Lornoxicam, derivs. 71002-09-0D, Pirazolac, derivs. 71125-38-7D, Meloxicam, derivs. 74103-06-3D, Ketorolac, derivs. 74711-43-6D, Zaltoprofen, derivs. 78499-27-1D, Bermoprofen, derivs. 78967-07-4D, Mofezolac, derivs. 91714-94-2D, Bromfenac, derivs. 92614-59-0D, Glutathione ethyl ester, derivs. 97473-82-0D, derivs. 99464-64-9D, Ampiroxicam, derivs. 156661-01-7 156970-83-1
158836-71-6 164790-48-1 170591-17-0 174454-43-4 175033-36-0
204268-63-3 290335-36-3 302543-75-5 311336-58-0 311336-60-4
311336-61-5 326850-30-0 497818-52-7 497818-53-8 497818-54-9
612478-19-0D, derivs. 612478-20-3D, derivs. 612478-21-4D, derivs.
612478-22-5D, derivs. 612478-23-6D, derivs. 612478-24-7D, derivs.
612478-25-8D, derivs. 612478-26-9D, derivs. 612478-27-0D, derivs.
612478-28-1 612478-29-2 612478-30-5 612478-31-6 612478-32-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nitrooxy derivs. of antiinflammatory/analgesic compds. for treatment of arthritis)

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 19 OF 32 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:742551 ZCAPLUS Full-text
DOCUMENT NUMBER: 140:104870
TITLE: Nitric oxide-releasing aspirin inhibits vasoconstriction in perfused tail artery of normotensive and spontaneously hypertensive rats
AUTHOR(S): Rossoni, Giuseppe; Manfredi, Barbara; Del Soldato, Piero; Polvani, Gianluca; Berti, Ferruccio
CORPORATE SOURCE: Department of Pharmacological Sciences, University of Milan, Milan, Italy
SOURCE: European Journal of Pharmacology (2003), 477(1), 59-68 CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The aim of this study was to investigate the capacity of the 2-(acetyloxy)benzoic acid 3-(nitrooxymethyl)phenyl ester (NCX 4016), a nitric oxide (NO)-releaser derivative of aspirin, to decrease blood pressure in spontaneously hypertensive rats (SHR) and to counteract the adrenergic vasoconstriction in perfused tail artery of these animals. Oral treatment for 10 consecutive days with NCX 4016 (100 μmol/kg) in SHR and their genetic controls Wistar Kyoto (WKY) rats resulted in a reduction of blood pressure in SHR but not in WKY rats. In SHR, the NCX 4016 treatment increased the serum nitrite/nitrate and diminished the serum thromboxane B2, whereas aspirin did not change blood pressure but abolished the serum thromboxane B2. Perfused tail arteries excised from vehicle-treated SHR exhibited a significant

impairment of endothelium-dependent vasorelaxant function. These vessels, prepared from SHR or WKY rats treated orally with NCX 4016 (10, 30 and 100 μmol/kg for 7 consecutive days), revealed a dose-dependent decrease in vasoconstriction in response to transmural nerve stimulation and norepinephrine, whereas aspirin was ineffective. Furthermore, in tail arteries of both SHR and WKY rats treated orally with NCX 4016 (100 μmol/kg for 7 consecutive days), the cGMP increased significantly. In conclusion, NCX 4016, by releasing NO and increasing cGMP in vascular tissue, reduces sympathetic-mediated vasoconstriction in resistance vessels and lowers blood pressure in SHR.

CC 1-8 (Pharmacology)
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

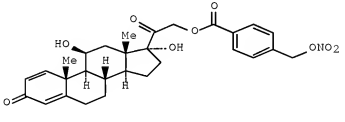
L31 ANSWER 20 OF 32 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:695997 ZCAPLUS Full-text
DOCUMENT NUMBER: 139:271224
TITLE: Glucocorticoid receptor nitration leads to enhanced anti-inflammatory effects of novel steroid ligands
AUTHOR(S): Paul-Clark, Mark J.; Roviezzo, Fiorentina; Flower, Roderick J.; Cirino, Giuseppe; Del Soldato, Piero; Adcock, Ian M.; Perretti, Mauro
CORPORATE SOURCE: The William Harvey Research Institute, Queen Mary School of Medicine and Dentistry, London, UK
SOURCE: Journal of Immunology (2003), 171(6), 3245-3252 CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English
AB It has recently emerged that posttranslational modification of proteins via nitration of tyrosine residues can alter their function. In this study, the authors describe that specific nitration of the glucocorticoid receptor (GR) by NCX-1015, a novel NO-donating prednisolone derivative (prednisolone 21-[4'-nitrooxymethyl]benzoate), results in an enhancement of GR-mediated events. Incubation of PBMC and U937 cells with 1-10 μM NCX-1015 caused faster activation of GR as assessed by augmented binding to [3H]dexamethasone, dissociation from heat shock protein 90, and nuclear translocation. PBMCs treated with NCX-1015 contained GR that had undergone tyrosine nitration. The chemical facilitating the increase in steroid binding capacity observed with NCX-1015 is specific, because changing the position of the NO-donating group or ubiquitous nitration by addition of an NO donor was unable to mimic this event. In vivo treatment with NCX-1015 provoked GR nitration and faster heat shock protein 90 dissociation as assessed in peritoneal cells. Accordingly, NCX-1015, but not prednisolone or other derivs., produced a rapid inhibition of the early neutrophil recruitment and mediator generation in a model of peritonitis. In conclusion, the authors report for the first time that posttranslational modification of GR by this novel nitrosteroid is associated with its enhanced anti-inflammatory activity.
CC 2-4 (Mammalian Hormones)
Section cross-reference(s): 1
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 21 OF 32 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:610468 ZCAPLUS Full-text
DOCUMENT NUMBER: 139:149818
TITLE: Preparation of new corticosteroids with glucocorticoid receptor affinity
INVENTOR(S): Del Soldato, Piero; Ongini, Ennio

PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003064443	A2	20030807	WO 2003-EP394	20030116
WO 2003064443	A3	20040226		
W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CR, CU, CZ, DM, DZ, EC, EE, GD, GE, HR, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, OM, PH, PL, RO, SC, SG, SK, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IT 2002MI0148	A1	20030729	IT 2002-MI148	20020129
CA 2473249	A1	20030807	CA 2003-2473249	20030116
EP 1470150	A2	20041027	EP 2003-734674	20030116
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003007027	A	20041103	BR 2003-7027	20030116
JP 2005516070	T	20050602	JP 2003-564063	20030116
NZ 534147	A	20060929	NZ 2003-534147	20030116
AU 2003210161	B2	20081204	AU 2003-210161	20030116
MX 2004007337	A	20041126	MX 2004-7337	20040729
NO 2004003595	A	20041020	NO 2004-3595	20040827
US 20060052594	A1	20060309	US 2005-501335	20050520
AU 2008258133	A1	20090108	AU 2008-258133	20081215
PRIORITY APPLN. INFO.:			IT 2002-MI148 A	20020129
			AU 2003-210161 A3	20030116
			WO 2003-EP394 W	20030116

OTHER SOURCE(S): MARPAT 139:149818
GI



II

AB Nitrooxy derivs. of steroidal compds. of formula B-X1-NO2 (I) or esters or salts thereof [B = steroidal radical; X1 = bivalent linking group comprising an aromatic or heterocyclic ring] are prepared The compds. have improved receptor affinity, antiinflammatory activity at peripheral level, and pharmacol. activity with lower side effects. Thus, II was prepared from prednisolone, 4-(chloromethyl)benzoyl chloride and silver nitrate. II showed strong antiinflammatory activity in the arthritis caused by collagen in rats.

IC ICM C07J
CC 32-5 (Steroids)
Section cross-reference(s): 1, 63
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 22 OF 32 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:133017 ZCAPLUS Full-text
DOCUMENT NUMBER: 138:163547
TITLE: Nitrooxy compounds for treatment of vasculopaties
INVENTOR(S): Del Soldato, Piero
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003013499	A2	20030220	WO 2002-EP8374	20020726
WO 2003013499	A3	20031231		
W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CR, CU, CZ, DM, DZ, EC, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, OM, PH, PL, RO, SG, SI, SK, TN, TR, TT, UA, US, UZ, VN, YU, ZA				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IT 2001MI1744	A1	20030210	IT 2001-MI1744	20010809
AU 2002333276	A1	20030224	AU 2002-333276	20020726
PRIORITY APPLN. INFO.:			IT 2001-MI1744 A	20010809
			WO 2002-EP8374 W	20020726

OTHER SOURCE(S): MARPAT 138:163547
AB The invention discloses the use for vasculopathy treatment of nitrooxy compds. (Markush included), or salts thereof. Compds. of the invention include e.g. 2-fluoro-α-methyl-4-diphenylacetic acid (4-nitrooxy)butyl ester (NO-flurbiprofen).
IC ICM A61K031-21
ICS A61K031-435; A61P007-00; A61P009-00
CC 1-8 (Pharmacology)
ST nitrooxy ester drug vasculopathy; flurbiprofen nitrooxy deriv vasculopathy drug
IT Carboxylic acids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hydroxy; nitrooxy compds. for treatment of vasculopaties)
IT Blood vessel, disease
Cardiovascular agents
(nitrooxy compds. for treatment of vasculopaties)
IT Amino acids, biological studies
Carboxylic acids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(nitrooxy compds. for treatment of vasculopaties)
IT Drug delivery systems
(oral; nitrooxy compds. for treatment of vasculopaties)
IT Drug delivery systems
(parenterals; nitrooxy compds. for treatment of vasculopaties)

IT Alcohols, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(polyhydric, aromatic and heterocyclic; nitrooxy compds. for treatment of vasculopaties)
IT Artery, disease
(restenosis; nitrooxy compds. for treatment of vasculopaties)
IT 290335-35-2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(46nitrooxy compds. for treatment of vasculopaties)
IT 50-81-7, Ascorbic acid, biological studies 52-67-5, Penicillamine 52-90-4, Cysteine, biological studies 57-50-1, Saccharose, biological studies 60-00-4, Edetic acid, biological studies 70-18-8D, Glutathione, esters 77-92-9, Citric acid, biological studies 80-72-8, Reductic acid 89-65-6, Isoascorbic acid 110-17-8, Fumaric acid, biological studies 111-17-1, 3,3'-Thiodipropionic acid 117-39-5, Quercetin 120-05-8, Sulphuretin 121-34-6, Vanillic acid 121-79-9, Propyl gallate 123-31-9, Hydroquinone, biological studies 149-91-7, Gallic acid, biological studies 154-23-4, Catechin 303-45-7, Gossypol 305-84-0, L-Carnosine 315-30-0, Allopurinol 331-39-5, Caffeic acid 458-35-5, Coniferyl alcohol 490-79-9, Gentisic acid 500-38-9, Nordihydroguaiaretic acid 501-94-0 520-18-3, Kaempferol 526-84-1, Dihydroxymaleic acid 533-73-3, Hydroxyhydroquinone 584-85-0, Anserine 616-91-1, N-Acetylcysteine 824-46-4, Methoxyhydroquinone 1078-61-1, Dihydrocaffeic acid 1135-24-6, Ferulic acid 1464-42-2, Selenomethionine 3614-08-2, Selenocysteine 3690-05-9, p-Cumaric alcohol 7400-08-0, p-Cumaric acid 15537-71-0, N-Acetylpenicillamine 63147-28-4, 3,5-Di-tert-butyl-4-hydroxybenzylthioglycolate 92614-59-0, Glutathione ethyl ester 97451-46-2, Glutathione isopropyl ester
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(nitrooxy compds. for treatment of vasculopaties)
IT 5104-49-4, Flurbiprofen 164790-48-1
RL: PAC (Pharmacological activity); BIOL (Biological study)
(nitrooxy compds. for treatment of vasculopaties)
IT 5104-49-4D, Flurbiprofen, nitrooxy derivs. 15307-86-5D, Diclofenac, nitrooxy derivs. 22204-53-1D, Naproxen, nitrooxy derivs. 156661-01-7 158836-71-6 163133-43-5 290335-26-1 302543-75-5 302543-79-9 410071-57-7 475561-43-4 497818-52-7 497818-53-8 497818-54-9 497818-55-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nitrooxy compds. for treatment of vasculopaties)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 23 OF 32 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:5915 ZCAPLUS Full-text
DOCUMENT NUMBER: 138:73081
TITLE: Preparation of nitrate esters of amino acids, hydroxyacids, and polyols as antiepileptics.
INVENTOR(S): Ongini, Ennio; Del Soldato, Piero
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2003000643	A1	20030103	WO 2002-EP6389	20020611
W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CR, CU, CZ, DM, DZ, EC, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, OM, PH, PL, RO, SG, SI, SK, TN, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IT 2001MI1307	A1	20021223	IT 2001-MI1307	20010621
AU 2002314157	A1	20030108	AU 2002-314157	20020611
PRIORITY APPLN. INFO.:			IT 2001-MI1307 A	20010621
			WO 2002-EP6389 W	20020611

OTHER SOURCE(S): MARPAT 138:73081

AB ABbDdNO2 [b, d = 0, 1; b, d cannot both = 0; A = RT1; R = R0R1R2W(CH2)m; W = C, N; m, n = 0-2; R0 = H, (CH2)nNHR1a; R1a = H, COR1h, CO2R1h; R1h = alkyl, Ph, PhCH2, etc.; R1 = H, electron pair; R2 = (substituted) Ph, PhCH2, amidino, etc.; B = TbX2Tbi; Tb = CO, X; Tbi = (CO)tx, Xtxx; tx, txx = 0, 1; X2 = bivalent radical; D = TcY; Tc = CO, X; Y = alkyleneoxy, cycloalkylene, [CH2CH(ONO2)CH2O]nf, (CH2)n3C6H4(CH2)n3IO, etc.; nf = 1-6; n3 = 0-5; n31 = 1-3; with provisos], were prepared as antiepileptics (no data). Thus, 1-(N-tert-butoxycarbonylaminomethyl)cyclohexaneacetic acid (preparation given), 2-methoxy-4-[(1E)-3-[4-(nitrooxy)butoxy]-3-oxy-1- propenyl]phenol (preparation given), dicyclohexylcarbodiimide, and N,N-dimethylaminopyridine were stirred 3 h at room temperature in CHCl3/DMF to give 1-(N-tert-butoxycarbonylaminomethyl)cyclohexaneacetic acid 2-methoxy-4-[(1E)-3-[4-(nitrooxy)butoxy]-3-oxy-1-propenyl]phenyl ester. This was stirred with HCl in EtOAc to give 1-(aminomethyl)cyclohexaneacetic acid 2-methoxy-4-[(1E)-3-[4-(nitrooxy)butoxy]-3-oxy-1-propenyl]phenyl ester hydrochloride.

IC ICM C07C203-04
ICS C07C229-28; C07C229-08; C07C327-22; C07C335-08; C07D213-30; C07C279-14; C07C279-12; A61K031-195; A61K031-155

CC 25-17 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1, 33, 34

ST nitrate ester amino acid hydroxyacid polyol prepn antiepileptic; aminomethylcyclohexaneacetic acid methoxynitrooxybutoxyloxypropenylphenyl ester prepn antiepileptic

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 24 OF 32 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:5914 ZCAPLUS Full-text
DOCUMENT NUMBER: 138:66698
TITLE: Nitro-oxy compounds for the treatment of chronic pain
INVENTOR(S): Del Soldato, Piero; Ongini, Ennio
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003000642	A2	20030103	WO 2002-EP5166	20020510
WO 2003000642	A3	20030327		
W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CR, CU, CZ, DM, DZ, EC, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK,				

LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, OM, PH, PL, RO, SG, SI, SK, TN, TR, TT, UA, US, UZ, VN, YU, ZA
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

IT 2001MI1308	A1	20021223	IT 2001-MI1308		20010621
CA 2450538	A1	20030103	CA 2002-2450538		20020510
AU 2002344965	A1	20030108	AU 2002-344965		20020510
EP 1417165	A2	20040512	EP 2002-742986		20020510
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
US 20040171682	A1	20040902	US 2003-480805		20031219
US 7199141	B2	20070403			
US 20070161576	A1	20070712	US 2007-705752		20070214
US 20080113950	A1	20080515	US 2007-984151		20071114
PRIORITY APPLN. INFO.:			IT 2001-MI1308	A	20010621
			WO 2002-EP5166	W	20020510
			US 2003-480805	A3	20031219
			US 2007-705752	A3	20070214

OTHER SOURCE(S): MARPAT 138:66698

AB Nitro-oxy derivative compds. or salts thereof having the general formula A(B)b0(C)c0NO2 (b0, c0 = 0, 1; A = RT1; R = radical of analgesic drug for chronic pain, in particular for neuropathic pain; B is such that its precursor is selected from amino acids, hydroxyacids, polyalcs., compds. containing at least one acid function; C is a bivalent radical containing an aliphatic, heterocyclic or aromatic radical). Preparation of selected compds., e.g. 1-(aminomethyl)cyclohexaneacetic acid 3-(nitrooxymethyl)phenyl hydrochloride ester, is described.

IC ICM C07C203-04
ICS A61K031-21

CC 1-11 (Pharmacology)
Section cross-reference(s): 25

ST chronic pain treatment nitro oxy deriv prepn; neuropathic pain treatment nitro oxy deriv

IT Pain
(chronic; nitro-oxy compds. for treatment of chronic pain, and use with other agents)

IT Amino acids, biological studies
Carboxylic acids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(derivs.; nitro-oxy compds. for treatment of chronic pain, and use with other agents)

IT Carboxylic acids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydroxy, derivs.; nitro-oxy compds. for treatment of chronic pain, and use with other agents)

IT Nerve, disease
(neuropathy, neuropathic pain; nitro-oxy compds. for treatment of chronic pain, and use with other agents)

IT Analgesics
(nitro-oxy compds. for treatment of chronic pain, and use with other agents)

IT Nitro compounds
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nitro-oxy compds. for treatment of chronic pain, and use with other agents)

IT Drug delivery systems
(oral; nitro-oxy compds. for treatment of chronic pain, and use with other agents)
IT Drug delivery systems
(parenterals; nitro-oxy compds. for treatment of chronic pain, and use with other agents)
IT Alcohols, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyhydric, aromatic and heterocyclic, derivs.; nitro-oxy compds. for treatment of chronic pain, and use with other agents)
IT Drug interactions
(synergistic; nitro-oxy compds. for treatment of chronic pain, and use with other agents)
IT Drug delivery systems
(topical; nitro-oxy compds. for treatment of chronic pain, and use with other agents)
IT 50-78-2D, Aspirin, derivs. 103-90-2D, Paracetamol, derivs. 5104-49-4D, Flurbiprofen, derivs. 15307-86-5D, Diclofenac, derivs. 15687-27-1D, Ibuprofen, derivs. 22204-53-1D, Naproxen, derivs.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NO-donating; nitro-oxy compds. for treatment of chronic pain, and use with other agents)
IT 10102-43-9, Nitric oxide, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(donors; nitro-oxy compds. for treatment of chronic pain, and use with other agents)
IT 60142-96-3, Gabapentin
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(nitro-oxy compds. for treatment of chronic pain, and use with other agents)
IT 479673-78-4P
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nitro-oxy compds. for treatment of chronic pain, and use with other agents)
IT 479673-77-3P 479674-28-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nitro-oxy compds. for treatment of chronic pain, and use with other agents)
IT 50-47-5, Desipramine 50-47-5D, Desipramine, derivs. 50-48-6, Amitriptyline 50-49-7, Imipramine 50-81-7D, Ascorbic acid, derivs. 52-67-5D, Penicillamine, derivs. 52-90-4D, Cysteine, derivs. 57-50-1D, Saccharose, derivs. 59-92-7D, Dopa, derivs. 60-00-4D, Edetic acid, derivs. 70-18-8D, Glutathione, derivs. 72-69-5, Nortriptyline 72-69-5D, Nortriptyline, derivs. 74-79-3D, Arginine, derivs. 77-92-9D, Citric acid, derivs. 80-72-8D, Reductic acid, derivs. 89-65-6D, Isoascorbic acid, derivs. 110-17-8D, Fumaric acid, derivs. 111-17-1D, 3,3'-Thiodipropionic acid, derivs. 113-53-1, Dothiepin 117-39-5D, Quercetin, derivs. 120-05-8D, Sulfuretin, derivs. 121-34-6D, Vanillic acid, derivs. 121-79-9D, Propyl gallate, derivs. 123-31-9D, Hydroquinone, derivs. 149-91-7D, Gallic acid, derivs. 154-23-4D, Catechin, derivs. 298-46-4, Carbamazepine 298-46-4D, Carbamazepine,

derivs. 303-45-7D, Gossypol, derivs. 303-49-1, Clomipramine 305-84-0D, L-Carnosine, derivs. 306-60-5D, Agmatine, derivs. 315-30-0D, Allopurinol, derivs. 315-72-0, , Opipramol 315-72-0D, Opipramol, derivs. 331-39-5D, Caffeic acid, derivs. 438-60-8, Protriptyline 458-35-5D, Coniferyl alcohol, derivs. 490-79-9D, Gentisic acid, derivs. 500-38-9D, Nordihydroguaiaretic acid, derivs. 501-94-0D, derivs. 520-18-3D, Kaempferol, derivs. 526-84-1D, Dihydroxymaleic acid, derivs. 533-73-3D, Hydroxyhydroquinone, derivs. 584-85-0D, Anserine, derivs. 616-91-1D, N-Acetylcysteine, derivs. 739-71-9, Trimipramine 824-46-4D, Methoxyhydroquinone, derivs. 1078-61-1D, Dihydrocaffeic acid, derivs. 1135-24-6D, Ferulic acid, derivs. 1464-42-2D, Selenomethionine, derivs. 1668-19-5, Doxepin 3362-45-6, Noxiptilin 3614-08-2D, Selenocysteine, derivs. 3690-05-9D, p-Cumaric alcohol, derivs. 4498-32-2, Dibenzepin 4757-55-5, Dimetacrine 5118-29-6, Melitracen 5560-72-5, Iprindole 6600-40-4D, Norvaline, derivs. 7400-08-0D, p-Cumaric acid, derivs. 10321-12-7, Propizepine 14028-44-5, Amoxapine 14028-44-5D, Amoxapine, derivs. 15537-71-0D, N-Acetylpenicillamine, derivs. 23047-25-8, Lofepramine 24701-51-7, , Demexiptiline 24701-51-7D, Demexiptiline, derivs. 25451-15-4, Felbamate 25451-15-4D, Felbamate, derivs. 30223-48-4, Fluacizine 35941-65-2, Butriptyline 57574-09-1, Amineptine 57574-09-1D, Amineptine, derivs. 60142-96-3D, Gabapentin, derivs. 63147-28-4D, 3,5-Di-tert-butyl-4-hydroxybenzylthio glycolate, derivs. 68291-97-4, Zonisamide 68291-97-4D, Zonisamide, derivs. 68506-86-5D, Vigabatrin, derivs. 72797-41-2, Tianeptine 72797-41-2D, Tianeptine, derivs. 84057-84-1, Lamotrigine 84057-84-1D, Lamotrigine, derivs. 92614-59-0D, Glutathione ethyl ester, derivs. 97240-79-4, Topiramate 97240-79-4D, Topiramate, derivs. 97451-46-2D, Glutathione isopropyl ester, derivs. 115103-54-3, Tiagabine 115103-54-3D, Tiagabine, derivs. 148553-50-8D, Pregabalin, derivs. 156719-37-8D, derivs. 175033-36-0 479673-79-5 479673-80-8 479673-81-9 479673-82-0 479673-83-1 479673-84-2 479673-85-3 479673-86-4 479673-87-5 479673-88-6 479673-89-7 479673-90-0 479673-91-1 479673-93-3 479673-95-5 479673-97-7 479673-99-9 479674-01-6 479674-03-8 479674-05-0 479674-07-2 479674-09-4 479674-11-8 479674-13-0 479674-15-2 479674-17-4 479674-19-6 479674-21-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nitro-oxy compds. for treatment of chronic pain, and use with other agents)

IT 110-52-1, 1,4-Dibromobutane 620-24-6, 3-Hydroxybenzyl alcohol 1135-24-6, Ferulic acid 6600-40-4, L-Norvaline 7761-88-8, Silver nitrate, reactions 24424-99-5, Di-tert-butyl dicarbonate
RL: RCT (Reactant); RACT (Reactant or reagent)
(nitro-oxy compds. for treatment of chronic pain, and use with other agents)

IT 53308-95-5P 74597-04-9P, 3-(Bromomethyl)phenol 227626-60-0P 410071-23-7P 475561-36-5P 479674-22-1P 479674-23-2P 479674-25-4P 479674-26-5P 479674-27-6P 479674-29-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(nitro-oxy compds. for treatment of chronic pain, and use with other agents)

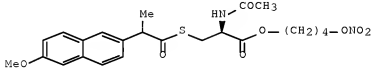
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 25 OF 32 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:888544 ZCAPLUS Full-text
DOCUMENT NUMBER: 137:369833
TITLE: Preparation of nitrooxy cysteine derivatives for the

Alzheimer's disease
INVENTOR(S): Del Soldato, Piero
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002092072	A2	20021121	WO 2002-EP5165	20020510
WO 2002092072	A3	20030501		
W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, ZA				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IT 2001MI0985	A1	20021115	IT 2001-MI985	20010515
AU 2002312897	A1	20021125	AU 2002-312897	20020510
PRIORITY APPLN. INFO.:			IT 2001-MI985 A	20010515
			WO 2002-EP5165 W	20020510

OTHER SOURCE(S): MARPAT 137:369833
GI



II

AB Title compds. A-Bn-Cm-NO2 [n, m = 0-1 with the proviso that m, n cannot be contemporaneously equal to 0; A = R-T1; R = (hetero)cycle; T1 = (CO)0-1, X0-1; X = O, S, amino; B = T2-X2-T3; T2-3 = CO, X, etc.; X2 = bivalent linking group; C = bivalent linking radical; I] were prepared For instance, 6-methoxy-α-methyl-2-naphthalenacetic acid was coupled to (S)-N-acetylcysteine (DMF/CHCl3, CDI, 12 h), the product converted to the 4-bromobutyl ester (THF, Ph3P, CBr4, 24 h) and that intermediate treated with AgNO3 (CH3CN, reflux, 7 h) to afford II. Nitrooxy derivs. of the invention are effective in inhibiting LPS-induced neurodegeneration and are useful in the treatment of Alzheimer's disease.

IC ICM A61K031-215
ICS A61K031-24; A61K031-404; A61K031-44; A61P025-28

CC 25-18 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1, 34, 63

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(lipopolysaccharide; preparation of nitrooxy cysteine derivs. and related analogs for Alzheimer's disease)

IT Alzheimer's disease

Anti-Alzheimer's agents
Anti-inflammatory agents
Human
(preparation of nitrooxy cysteine derivs. and related analogs for Alzheimer's disease)

IT Amino acids, preparation
Esters, preparation
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of nitrooxy cysteine derivs. and related analogs for Alzheimer's disease)

IT Esters, preparation
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(thio; preparation of nitrooxy cysteine derivs. and related analogs for Alzheimer's disease)

IT 158836-71-6P 301838-28-8P 302543-75-5P 302543-76-6P 302543-77-7P 302543-79-9P 475561-33-2P 475561-34-3P 475561-35-4P 475561-36-5P 475561-37-6P 475561-38-7P 475561-39-8P 475561-40-1P 475561-43-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of nitrooxy cysteine derivs. and related analogs for Alzheimer's disease)

IT 50-81-7, Ascorbic acid, reactions 52-67-5, Penicillamine 52-90-4, Cysteine, reactions 53-86-1 57-50-1, Saccharose, reactions 60-00-4, Edetic acid, reactions 70-18-8, Glutathione, reactions 77-92-9, Citric acid, reactions 80-72-8, Reductic acid 89-65-6, Isoascorbic acid 110-17-8, Fumaric acid, reactions 110-52-1, 1,4-Dibromobutane 111-17-1, 3,3'-Thiodipropionic acid 117-39-5, Quercetin 120-05-8, Sulphuretin 121-34-6, Vanillic acid 121-79-9, Propyl gallate 149-91-7, Gallic acid, reactions 154-23-4, Catechin 303-45-7, Gossypol 305-84-0, L-Carnosine 315-30-0, Allopurinol 331-39-5, Caffeic acid 458-35-5, Coniferyl alcohol 490-79-9, Gentisic acid 500-38-9, Nordihydroguaiaretic acid 501-94-0, 4-Hydroxyphenethyl alcohol 520-18-3, Kaempferol 522-66-7, Hydroquinine 526-84-1, Dihydroxymaleic acid 533-73-3, Hydroxyhydroquinone 584-85-0, Anserine 616-91-1, (S)-N-Acetylcysteine 824-46-4, Methoxyhydroquinone 1078-61-1, Dihydrocaffeic acid 1135-24-6, Ferulic acid 3211-76-5, Selenomethionine 3614-08-2, Selenocysteine 3690-05-9, p-Cumaric alcohol 7400-08-0, p-Cumaric acid 7761-88-8, Silver nitrate, reactions 15537-71-0, N-Acetylpenicillamine 15687-27-1 22204-53-1 62741-78-0 63147-28-4, 3,5-Di-tert-butyl-4-hydroxybenzylthioglycolate
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of nitrooxy cysteine derivs. and related analogs for Alzheimer's disease)

IT 301838-04-0P 301838-05-1P 301838-06-2P 301838-07-3P 301838-08-4P 301838-09-5P 475561-41-2P 475561-42-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of nitrooxy cysteine derivs. and related analogs for Alzheimer's disease)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 26 OF 32 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:383293 ZCAPLUS Full-text
DOCUMENT NUMBER: 137:320098

TITLE: Vascular protective actions of a nitric oxide aspirin analog in both in vitro and in vivo models of diabetes mellitus

AUTHOR(S): Pieper, Galen M.; Siebeneich, Wolfgang; Olds, Cara L.; Felix, Christopher C.; Del Soldato, Piero

CORPORATE SOURCE: Division of Transplant Surgery, Medical College of Wisconsin, Milwaukee, WI, USA

SOURCE: Free Radical Biology & Medicine (2002), 32(11), 1143-1156
CODEN: FRBMEH; ISSN: 0891-5849

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Background: Defective endothelium-dependent relaxation is observed in exptl. and human diabetes mellitus. The nature of this defect is not fully understood but may involve decreased NO bioactivity due to enhanced production of reactive oxygen species (ROS). In this paper, the authors examine the benefits and actions of a novel NO-donating, antioxidant called 2-acetoxybenzoic acid 2-(2-nitrooxymethyl) Ph ester, and denoted as NCX4016, on NO-mediated endothelium-dependent relaxation in normal arteries exposed to acute elevations in glucose or in arteries derived from chronic diabetic animals. Material and Methods: Intrinsic free radical scavenging by NO-NSAIDs in solution were evaluated using ESR (EPR) spectroscopy and spin trapping with 5,5-dimethyl-1-pyrroline-N-oxide (DMPO). In acute studies, normal rat aortas were exposed in tissue culture for 18 h to 5.5 or 40 mM in the presence or absence of NCX4016, a NO-donating NSAID unrelated to aspirin (NCX2216), or aspirin. Vascular reactivity of thoracic aortic rings to endothelium-dependent relaxation to acetylcholine in vitro was determined For chronic hyperglycemia, diabetes was induced in rats by i.v. injection with streptozotocin. Vascular reactivity of thoracic aortic rings to endothelium-dependent relaxation to acetylcholine in vitro was determined after 8 wk in untreated animals or animals chronically-treated with NCX4016. Antioxidant efficacy in vivo was determined by measurement of plasma isoprostanes and by nuclear binding activity of NF-κB in nuclear fractions of aorta. Results: Incubation with NCX4016 and NCX2216 produced a concentration-dependent inhibition of DMPO-OH formation indicating scavenging of hydroxyl radicals (HO•). In contrast, little efficacy to scavenge superoxide anion radicals was noted. Acute incubation of normal arteries with elevated glucose concentration caused inhibition of normal relaxation to acetylcholine. This impairment was prevented by co-incubation with NCX4106 but not by mannitol, the parent compound (aspirin), or by NCX2216. In addition, chronic treatment with NCX4016 prevented the development of defective endothelium-dependent relaxation to acetylcholine. This protection did not occur as a result to any changes in blood glucose concentration or Hb glycation. Treatment with NCX4016 did decrease the elevation in plasma isoprostanes and normalized the diabetes-induced increase in NF-κB binding activity in nuclear fractions derived from aortic tissue. Conclusions: Collectively, these studies suggest that antioxidant interventions using NO-donating NSAIDs may provide an important novel therapeutic strategy to protect the diabetic endothelium.

CC 1-8 (Pharmacology)
Section cross-reference(s): 2

REFERENCE COUNT: 85 THERE ARE 85 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 27 OF 32 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:293592 ZCAPLUS Full-text

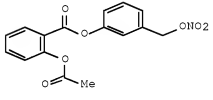
DOCUMENT NUMBER: 136:325420

TITLE: Drugs for diabetes, especially type 2, comprising an antiinflammatory or analgesic drug, selected bivalent

linkers, and a nitrate ester
INVENTOR(S): Del Soldato, Piero
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002030867	A2	20020418	WO 2001-EP11665	20011009
WO 2002030867	A3	20020725		
W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IT 2000MI2201	A1	20020412	IT 2000-MI2201	20001012
IT 1319201	B1	20030926		
CA 2425655	A1	20020418	CA 2001-2425655	20011009
AU 2002014006	A	20020422	AU 2002-14006	20011009
EP 1324974	A2	20030709	EP 2001-982414	20011009
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004511456	T	20040415	JP 2002-534256	20011009
US 20040023890	A1	20040205	US 2003-398511	20030411
US 7378437	B2	20080527		

PRIORITY APPLN. INFO.: IT 2000-MI2201 A 20001012
WO 2001-EP11665 W 20011009
OTHER SOURCE(S): MARPAT 136:325420
GI



II

AB Useful for the treatment of diabetes, particularly type 2, are compds. or salts thereof, having the following general formula A-(B)n-(C)m-NO2 [I; wherein A = radical of a drug having an antiinflammatory or analgesic activity; B = bivalent linking group wherein the precursor must meet certain tests described in the application; C = another defined bivalent linking group; n and m = 0 or 1, provided that (n + m) = 1 or 2]. I can be used in conjunction with other antidiabetic drugs, particularly insulin. I increase the direct antidiabetic effect of insulin, and reduce complications of diabetes, particularly vascular diseases, retinopathies, neuropathies, etc.. The values of n and m, i.e., the presence or absence of bivalent linkers B and C, alone or in combination, are based on performance of the precursors of the

linkers in certain tests (no data). These tests are designated as follows: (test 4A): inhibition by > 15% of hemolysis of rat erythrocytes induced by cumene hydroperoxide; (test 5): inhibition of radical production by ≥ 50% in the oxidative degradation of . desoxyribose in aqueous Fe2+(NH4)2(SO4)2/thiobarbituric acid solution; and (test 4): inhibition by ≥ 50% of DPPH-induced radical production in MeOH solution For instance, acetylsalicylic acid chloride was esterified with 3-(hydroxymethyl)phenol (80%), followed by nitation of the resultant Ph ester with HNO3/H2SO4 (82%), to give invention compound II, which is thus the 3-(nitrooxymethyl)phenyl ester of aspirin. When tested on isolated aorta from insulin-resistant rats, compound II at a concentration of 10-4 M gave 70% vasorelaxation, relative to non-insulin-resistant controls. This effect was unchanged by the presence or absence of the irreversible NO synthetase inhibitor LNNA. In contrast, both Na nitroprussiate and the indomethacin analog of II, known NO donors, were inactive, and the antidiabetic drug metformin was inactivated by LNNA.

IC ICM C07C203-04
ICS A61K031-04; A61K031-621; A61P003-10

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

IT 290335-23-8P, 2-Acetyloxybenzoic acid [6-(nitrooxymethyl)-2-pyridinyl]methyl ester
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of antidiabetic agents comprising antiinflammatory or analgesic drugs, selected bivalent linkers, and nitrate esters)

IT 175033-36-0P, 2-Acetoxybenzoic acid 3-nitrooxymethylphenyl ester 287118-97-2P, 2-(Acetyloxy)benzoic acid 4-(nitroxymethyl)phenyl ester 290335-22-7P, 2-Acetoxybenzoic acid [6-(nitroxymethyl)-2-pyridinyl]methyl ester hydrochloride 290335-24-9P, 2-Acetyloxybenzoic acid [6-(nitrooxymethyl)-2-pyridinyl]methyl ester nitrate 302543-76-6P 410071-13-5P, 2-(Acetyloxy)benzoic acid [3-(nitrooxymethyl)-2-pyridinyl]methyl ester hydrochloride 410071-14-6P, trans-3-[4-[2-(Acetyloxy)benzoyloxy]-3-methoxyphenyl]-2-propenoic acid 4-(nitroxy)butyl ester 410071-38-4P, 2-Acetyloxybenzoic acid [5-(nitrooxymethyl)-2-pyridinyl]methyl ester hydrochloride 410071-40-8P, 2-Acetyloxybenzoic acid [5-(nitrooxymethyl)-2-pyridinyl]methyl ester nitrate 410071-45-3P, 2-(Acetyloxy)benzoic acid [3-(nitrooxymethyl)-2-pyridinyl]methyl ester nitrate
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of antidiabetic agents comprising antiinflammatory or analgesic drugs, selected bivalent linkers, and nitrate esters)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 28 OF 32 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:293591 ZCAPLUS Full-text
DOCUMENT NUMBER: 136:309852
TITLE: Preparation of nitrooxyalkylarenes as antiinflammatories and anticancer drugs.
INVENTOR(S): Del Soldato, Piero; Benedini, Francesca; Antognazza, Patrizia
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002030866	A1	20020418	WO 2001-EP11664	20011009
W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IT 2000MI2202	A1	20020412	IT 2000-MI2202	20001012
IT 1319202	B1	20030926		
CA 2425649	A1	20020418	CA 2001-2425649	20011009
AU 2002015932	A	20020422	AU 2002-15932	20011009
EP 1339665	A1	20030903	EP 2001-986670	20011009
EP 1339665	B1	20071219		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004511455	T	20040415	JP 2002-534255	20011009
AT 381531	T	20080115	AT 2001-986670	20011009
ES 2298280	T3	20080516	ES 2001-986670	20011009
US 20040023933	A1	20040205	US 2003-398289	20030410
US 7465803	B2	20081216		
US 20080194651	A1	20080814	US 2008-99636	20080408
US 20090075952	A1	20090319	US 2008-271440	20081114

PRIORITY APPLN. INFO.:		IT 2000-MI2202	A	20001012
		WO 2001-EP11664	W	20011009
		US 2003-398289	A3	20030410

OTHER SOURCE(S): MARPAT 136:309852

AB AX1LWpNO2 [p = 0, 1; A = RT1; R = specified precursor drug radicals; T1 = (CO)t, Xtt; X = O, S, imino, etc.; X1 = TbYTbb; Tb = CO, X; Tbb = (CO)xx, Xxxx; t, tt, xx, xxx = 0, 1; Y, Yt = specified bivalent linker; W = YtO; with provisos], were prepared Thus, acetylsalicylic acid in DMF was treated with NaOEt; after 30 min. the solution was added to a solution of bis(chloromethyl)pyridine (preparation given) in DMF; the mixture was kept 7 days to give 2-acetyloxybenzoic acid 6-chloromethyl-2-methylpyridinyl ester. The latter was heated with AgNO3 in MeCN at 80° for 30 min. to give 2-acetyloxybenzoic acid 6-nitrooxymethyl-2-methylpyridinyl ester. The latter at 10 μM gave 100% inhibition of HT29 cancer cells.

IC ICM C07C203-04
ICS C07C233-54; C07C323-60; C07D201-02; C07C317-46; A61K031-21; C07D213-34; A61K031-44

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

ST nitrooxyalkylarene prepn antiinflammatory; anticancer nitrooxyalkyl arene prepn; hepatoprotectant nitrooxyalkylarene prepn

IT Cytoprotective agents
(hepatoprotective agents; preparation of nitrooxyalkylarenes as antiinflammatories and anticancer drugs)

IT Anti-inflammatory agents
Antitumor agents
Human
(preparation of nitrooxyalkylarenes as antiinflammatories and anticancer drugs)

IT 287118-96-1P 287118-97-2P 290335-22-7P 290335-23-8P 290335-24-9P 302543-78-8P 302543-79-9P 302606-04-8P 326850-30-0P 326850-47-9P

410071-13-5P 410071-14-6P 410071-15-7P 410071-16-8P 410071-17-9P
410071-18-0P 410071-19-1P 410071-20-4P 410071-21-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of nitrooxyalkylarenes as antiinflammatories and anticancer drugs)

IT 175033-36-0 290335-26-1 290335-35-2 302543-75-5 410071-33-9
410071-34-0 410071-35-1 410071-37-3 410071-38-4 410071-40-8
410071-41-9 410071-43-1 410071-45-3 410071-46-4 410071-48-6
410071-49-7 410071-50-0 410071-51-1 410071-52-2 410071-53-3
410071-54-4 410071-55-5 410071-56-6 410071-57-7 410071-58-8
410071-59-9 410071-60-2 410071-61-3 410071-63-5 410071-65-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of nitrooxyalkylarenes as antiinflammatories and anticancer drugs)

IT 50-78-2, Acetylsalicylic acid 90-02-8, 2-Hydroxybenzaldehyde, reactions 103-90-2, Paracetamol 110-52-1, 1,4-Dibromobutane 123-08-0, 4-Hydroxybenzaldehyde 612-20-4, 2-Hydroxymethylbenzoic acid 616-91-1, N-Acetylcysteine 620-24-6, 3-Hydroxymethylphenol 876-08-4, 4-(Chloromethyl)benzoylchloride 927-58-2, 4-Bromobutyryl chloride 1135-24-6, Ferulic acid 1195-59-1, 2,6-Bis(hydroxymethyl)pyridine 2623-87-2, 4-Bromobutyric acid 5538-51-2, Acetylsalicylic acid chloride 15687-27-1 21514-99-8, 2,5-Bis(hydroxymethyl)pyridine 38070-79-0, 2,3-Bis(hydroxymethyl)pyridine 38194-50-2, Sulindac 42908-86-1 55882-65-0 89211-34-7, 3-[(2-Hydroxy)ethoxy]propanoic acid 175077-14-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of nitrooxyalkylarenes as antiinflammatories and anticancer drugs)

IT 3099-28-3P, 2,6-Bis(chloromethyl)pyridine 34749-55-8P 45754-12-9P, 2,3-Bis(chloromethyl)pyridine 94126-97-3P, 2,5-Bis(chloromethyl)pyridine 132520-62-8P 132521-15-4P 203065-56-9P 287118-98-3P 290335-38-5P 301828-34-2P 301838-10-8P 301838-11-9P 410071-22-6P 410071-23-7P 410071-24-8P 410071-25-9P 410071-26-0P 410071-27-1P 410071-28-2P 410071-29-3P 410071-30-6P 410071-31-7P 410071-32-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of nitrooxyalkylarenes as antiinflammatories and anticancer drugs)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 29 OF 32 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:561195 ZCAPLUS Full-text
DOCUMENT NUMBER: 135:327311
TITLE: NCX-1000, a NO-releasing derivative of ursodeoxycholic acid, selectively delivers NO to the liver and protects against development of portal hypertension
AUTHOR(S): Fiorucci, Stefano; Antonelli, Elisabetta; Morelli, Olivia; Mencarelli, Andrea; Casini, Alessandro; Mello, Tommaso; Palazzetti, Barbara; Tallet, Dominique; Del Soldato, Piero; Morelli, Antonio
CORPORATE SOURCE: Clinica di Gastroenterologia ed Epatologia, Dipartimento di Medicina Clinica e Sperimentale, Universita degli Studi di Perugia, Perugia, 06122, Italy
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2001), 98(15), 8897-8902
CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Portal hypertension resulting from increased intrahepatic resistance is a common complication of chronic liver diseases and a leading cause of death in patients with liver cirrhosis, a scarring process of the liver that includes components of both increased fibrogenesis and wound contraction. A reduced production of nitric oxide (NO) resulting from an impaired enzymic function of endothelial NO synthase and an increased contraction of hepatic stellate cells (HSCs) have been demonstrated to contribute to high intrahepatic resistance in the cirrhotic liver, 2-(Acetyloxy)benzoic acid 3-(nitrooxymethyl)Ph ester (NCX-1000) is a chemical entity obtained by adding an NO-releasing moiety to ursodeoxycholic acid (UDCA), a compound that is selectively metabolized by hepatocytes. In this study we have examined the effect of NCX-1000 and UDCA on liver fibrosis and portal hypertension induced by i.p. injection of carbon tetrachloride in rats. Our results demonstrated that although both treatments reduced liver collagen deposition, NCX-1000, but not UDCA, prevented ascite formation and reduced intrahepatic resistance in carbon tetrachloride-treated rats as measured by assessing portal perfusion pressure. In contrast to UDCA, NCX-1000 inhibited HSC contraction and exerted a relaxing effect similar to the NO donor S-nitroso-N-acetylpenicillamine. HSCs were able to metabolize NCX-1000 and release nitrite/nitrate in cell supernatants. In aggregate these data indicate that NCX-1000, releasing NO into the liver microcirculation, may provide a novel therapy for the treatment of patients with portal hypertension.

CC 1-12 (Pharmacology)
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 30 OF 32 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:176536 ZCAPLUS Full-text
DOCUMENT NUMBER: 135:14275
TITLE: An NO derivative of ursodeoxycholic acid protects against Fas-mediated liver injury by inhibiting caspase activity
AUTHOR(S): Fiorucci, Stefano; Mencarelli, Andrea; Palazzetti, Barbara; Del Soldato, Piero; Morelli, Antonio; Ignarro, Louis J.
CORPORATE SOURCE: Dipartimento di Medicina Clinica e Sperimentale, Clinica di Gastroenterologia ed Epatologia, Universita degli Studi di Perugia, Perugia, 06122, Italy
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2001), 98(5), 2652-2657
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Caspases are key mediators in liver inflammation and apoptosis. In the present study we provide evidence that a nitric oxide (NO) derivative of ursodeoxycholic acid (UDCA), NCX-1000 ([2-(acetyloxy)benzoic acid 3-(nitrooxymethyl)phenyl ester]), protects against liver damage in murine models of autoimmune hepatitis induced by i.v. injection of Con A or a Fas agonistic antibody, Jo2. Con A administration causes CD4+ T lymphocytes to accumulate in the liver and up-regulates FasL expression, resulting in FasL-mediated cytotoxicity. Cotreating mice with NCX-1000, but not with UDCA, protected against liver damage induced by Con A and Jo2, inhibited IL-1β, IL-18, and IFN-γ release and caspase 3, 8, and 9 activation. Studies on HepG2 cells demonstrated that NCX-1000, but not UDCA, directly prevented multiple caspase activation induced by Jo2. Incubating HepG2 cells with NCX-1000 resulted in intracellular NO formation and a DTT-reversible inhibition of proapoptotic

caspases, suggesting that cysteine S-nitrosylation was the main mechanism responsible for caspase inhibition. Collectively, these data suggest that NCX-1000 protects against T helper 1-mediated liver injury by inhibiting both the proapoptotic and the proinflammatory branches of the caspase superfamily.
CC 1-12 (Pharmacology)
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 31 OF 32 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:898365 ZCAPLUS Full-text
DOCUMENT NUMBER: 134:188313
TITLE: 21-NO-prednisolone is a novel nitric oxide-releasing derivative of prednisolone with enhanced anti-inflammatory properties
AUTHOR(S): Paul-Clark, Mark; Del Soldato, Piero; Fiorucci, Stefano; Flower, Roderick J.; Perretti, Mauro
CORPORATE SOURCE: Department of Biochemical Pharmacology, St Bartholomew's and the Royal London School of Medicine and Dentistry, London, UK
SOURCE: British Journal of Pharmacology (2000), 131(7), 1345-1354
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The anti-inflammatory effects of a novel derivative of the glucocorticoid prednisolone were investigated. NCX-1015 (prednisolone 21-[(4'-nitrooxymethyl)benzoate]) incubation in human platelet-rich plasma produced at a time- and concentration-dependent release of nitrite, that was mirrored by accumulation of cyclic guanosine monophosphate in the human platelets. I.p. injection of NCX-1015 to mice produced nitrite accumulation in the peritoneal cavity. Findings indicated that NCX-1015 is more potent than prednisolone in controlling several, though not all, parameters of acute and chronic inflammation. It is proposed that this effect may be due to a cooperation between the steroid moiety and nitric oxide or related species released in biol. fluids. It is suggested that NCX-1015 is the first member of a novel class of anti-inflammatory compds., the nitro-steroids.
CC 2-4 (Mammalian Hormones)
Section cross-reference(s): 1
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

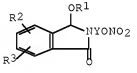
L31 ANSWER 32 OF 32 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1993:80802 ZCAPLUS Full-text
DOCUMENT NUMBER: 118:80802
ORIGINAL REFERENCE NO.: 118:14213a,14216a
TITLE: Preparation of (nitrooxyalkyl)isoindolinolones having cardiovascular activity
INVENTOR(S): Sala, Alberto; Levi, Silvio; Benedini, Francesca; Cereda, Roberta; Del Soldato Piero
PATENT ASSIGNEE(S): Italfarmaco S.p.A., Italy
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9216506	A1	19921001	WO 1992-EP531		19920311
W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD, US					
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG					
AU 9213479	A	19921021	AU 1992-13479		19920311
AU 659442	B2	19950518			
EP 576475	A1	19940105	EP 1992-906404		19920311
EP 576475	B1	19950920			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE					
JP 06505722	T	19940630	JP 1992-505510		19920311
HU 67668	A2	19950428	HU 1993-2507		19920311
AT 128123	T	19951015	AT 1992-906404		19920311
ES 2079185	T3	19960101	ES 1992-906404		19920311
NO 9303324	A	19930917	NO 1993-3324		19930917
US 5376673	A	19941227	US 1993-117162		19930917
PRIORITY APPLN. INFO.:			IT 1991-MI732	A	19910319
			WO 1992-EP531	A	19920311

OTHER SOURCE(S): MARPAT 118:80802

GI



I

AB Title compds. I (R1 = H, C1-6 alkyl, (substituted) PhCH2; R2, R3 = H, halo, C1-4 alkyl, F3C, HO, O2N, (monoalkyl)(dialkyl) amino, cyano, C1-6 alkoxy, C2-6 alkoxycarbonyl; Y = CH2CH2, C3-6 alkylene) or a salt thereof, are prepared Et chlorocarbonate was added to 2-(HO2C)C6H4CHO in CHCl3 and Et3N followed by ClCH2CH2NH2 to give 3-hydroxy-2-(2-chloroethyl)-1-oxoisoindoline to which in MeCN was added AgNO3 to give I (R1 = R2 = R3 = H, Y = CH2CH2) (II). In Arg-vasopressin-induced coronary spasm, II at 3 mg/kg by gastric gavage showed 56.1% reduction

IC ICM C07D209-48
ICS A61K031-40

CC 27-11 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

ST isoindolinolone nitrooxyalkyl prepn cardiovascular; antiangina nitrooxyalkylisoindolinolone

IT Cardiovascular agents
((nitrooxyalkyl)isoindolinolones)

IT Heart, disease
(angina pectoris, treatment of, (nitrooxyalkyl)isoindolinolones for)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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DICTIONARY FILE UPDATES:   6 MAY 2009  HIGHEST RN 1143575-54-5

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experimental property data in the original document.  For information
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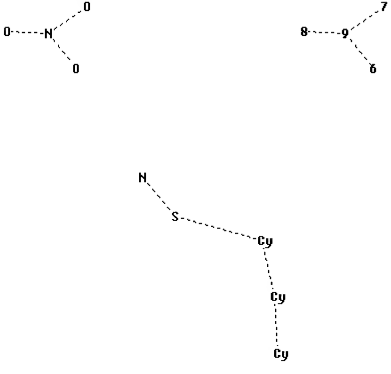


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chain bonds :
1-2  1-3  3-4  4-5  6-9  7-9  8-9
exact/norm bonds :
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1-2 1-3 3-4 4-5 6-9 7-9 8-9

Connectivity :
2:2 M minimum RC ring/chain
Match level :
1:CLASS 2:CLASS 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:CLASS

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FILE COVERS 1907 - 7 May 2009 VOL 150 ISS 19
FILE LAST UPDATED: 6 May 2009 (20090506/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2009

ZCAplus now includes complete International Patent Classification (IPC)
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substance identification.
'OBI' IS DEFAULT SEARCH FIELD FOR 'ZCAPLUS' FILE

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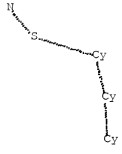


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L14           5 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  L13


=> d ibib abs hitstr L14 1-5

L14  ANSWER 1 OF 5  ZCAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:         2006:191976  ZCAPLUS  Full-text
DOCUMENT NUMBER:          144:273755
TITLE:                    Preparation of prodrugs containing novel biocleavable
                          linkers
INVENTOR(S):              Satyam, Apparao
PATENT ASSIGNEE(S):       Nicholas Piramal India Ltd., India
SOURCE:                   U.S. Pat. Appl. Publ., 181 pp.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
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     US 20060046967       A1    20060302    US 2005-213396          20050826
     US 20060205674       A2    20060914
     AU 2005281359        A1    20060316    AU 2005-281359          20050826
     CA 2577490           A1    20060316    CA 2005-2577490         20050826
     WO 2006027711        A2    20060316    WO 2005-IB52797         20050826
     WO 2006027711        A3    20070315
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
             LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
             NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
             SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
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ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

EP 1789091	A2	20070530	EP 2005-781464		20050826
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU					
CN 101039701	A	20070919	CN 2005-80034555		20050826
JP 2008510795	T	20080410	JP 2007-529100		20050826
BR 2005015218	A	20080708	BR 2005-15218		20050826
KR 2007053214	A	20070523	KR 2007-702931		20070206
MX 2007002210	A	20070507	MX 2007-2210		20070223
IN 2007MN00439	A	20070720	IN 2007-MN439		20070326
PRIORITY APPLN. INFO.:			US 2004-604632P	P	20040826
			IN 2005-MU779	A	20050701
			WO 2005-IB52797	W	20050826

OTHER SOURCE(S): CASREACT 144:273755; MARPAT 144:273755

AB The invention provides compds. D1-L1-E-A-B-A1-E-(L-E-A1-B-A-E)0-2-L2-D2 [B is a bond, (CH2)1-6, (CH2CH2O)1-1000, S-S, S-S:O, S-SO2 or S-S:NH; A, A1 are independently a bond, (CH2)1-8, 1,2-, 1,3- or 1,4-phenylene; D1 is a therapeutic agent having one or more functional groups OH, SH, NHR1, CO2H, CONHR1, O2CNHR1, SO2NHR1, SO2NHR1, NR1CONHNHR1 or NR1SO2NHR1 (R1 is H, alkyl, aryl, etc.); D2 is D1, a peptide, protein, monoclonal antibody, vitamin, NO, NO2, NONOate, a nitric oxide-releasing group, a polymer, etc.; E is independently CH2 or a bond; L1, L2 are independently a bond, O, S, NR1, L, or a linkage] or their pharmaceutically-acceptable salts for use as prodrugs, including NO-releasing prodrugs. Thus, aspirin prodrug 2-AcOC6H4CONHCH2CH2SSCH2CH2ONO2 was prepared and shown to release salicylate in rats in a sustained and controlled manner starting from 1 h through 12 h.

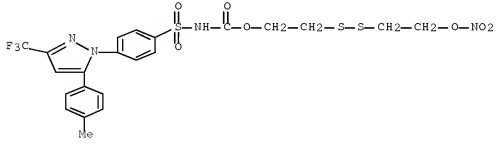
IT 877865-25-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of prodrugs containing novel biocleavable linkers)

RN 877865-25-3 ZCAPLUS

CN Carbamic acid, [[4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]phenyl]sulfonyl]-, 2-[[2-(nitrooxy)ethyl]dithio]ethyl ester (9CI) (CA INDEX NAME)



L14 ANSWER 2 OF 5 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:547257 ZCAPLUS Full-text

DOCUMENT NUMBER: 143:77866
TITLE: Preparation of nitrate esters having a β- or γ-sulfur atom for protection of cells/tissues from oxidative damage.
INVENTOR(S): Thatcher, Gregory R. j.; Bennett, Brian M.; Reynolds, James N.; Boegman, Roland J.; Jhamandas, Khem
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 83 pp., Cont.-in-part of U.S. Ser. No. 147,808.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20050137191	A1	20050623	US 2004-943264	20040917
US 5807847	A	19980915	US 1996-658145	19960604
US 5883122	A	19990316	US 1997-867856	19970603
US 6310052	B1	20011030	US 1999-267379	19990315
US 7115661	B1	20061003	US 1999-473713	19991229
EP 1518553	A2	20050330	EP 2004-28372	20001227
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
US 20020177622	A1	20021128	US 2002-147808	20020520
US 6916835	B2	20050712		
AU 2005284573	A1	20060323	AU 2005-284573	20050916
CA 2580627	A1	20060323	CA 2005-2580627	20050916
WO 2006029532	A1	20060323	WO 2005-CA1417	20050916
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1797100	A1	20070620	EP 2005-787832	20050916
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				

PRIORITY APPLN. INFO.:		
US 1996-658145	A2	19960604
US 1997-867856	A2	19970603
US 1999-267379	A3	19990315
US 1999-473713	A2	19991229
US 2002-147808	A2	20020520
EP 2000-986925	A3	20001227
US 2001-851591	A3	20010510
US 2002-108513	A3	20020329
US 2004-943264	A	20040917
WO 2005-CA1417	W	20050916

OTHER SOURCE(S): CASREACT 143:77866; MARPAT 143:77866

AB YXCR3R4(CR1′R18)n(CR1R2)mONO2 [m, n = 0-10; R3, R4, R17 = H, nitrate, A; R1 = H, A; A = (substituted) (unsatd.) (cyclic) aliphatyl; R1R3, R4R17 = aliphatyl linkage; R2, R18 = H, A, XY; X = F, Cl, Br, Cl, NO2, CH2, CF2, O, NH, NMe, cyano, NHOH, N3, S, SCN, SO, SO2, etc.; Y = null, F, Cl, Br, Cl, Me, CF2H,

CF3, OH, NH2, S, SCN, SH, etc.; with provisos], were prepared Thus, [O2NOCH2CH(ONO2)CH2S]2 (prepared via the corresponding Bunte salt) at 200 μmol/kg s.c. gave virtually complete protection against 6-OHDA killing of dopaminergic neurons in rats.

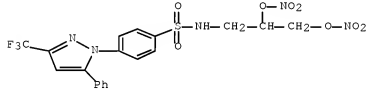
IT 854925-45-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(claimed compound; preparation of nitrate esters having β- or γ-sulfur atom for protection of cells/tissues from oxidative damage)

RN 854925-45-4 ZCAPLUS

CN Benzenesulfonamide, N-[2,3-bis(nitrooxy)propyl]-4-[5-phenyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (CA INDEX NAME)



L14 ANSWER 3 OF 5 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:370913 ZCAPLUS Full-text

DOCUMENT NUMBER: 140:375166

TITLE: Preparation of nitric oxide releasing selective cyclooxygenase-2 inhibitors

INVENTOR(S): Wang, Zhaoyin; Young, Robert N.; Zamboni, Robert

PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.

SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

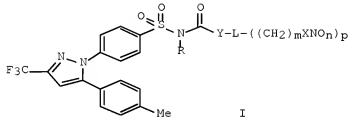
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004037798	A1	20040506	WO 2003-CA1605	20031021
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2503063	A1	20040506	CA 2003-2503063	20031021
AU 2003278039	A1	20040513	AU 2003-278039	20031021
EP 1562914	A1	20050817	EP 2003-769122	20031021
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

US 20060058363 A1 20060316 US 2005-530214 20050404
PRIORITY APPLN. INFO.: US 2002-420292P P 20021022
WO 2003-CA1605 W 20031021
OTHER SOURCE(S): MARPAT 140:375166
GI



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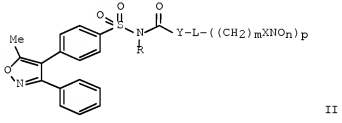


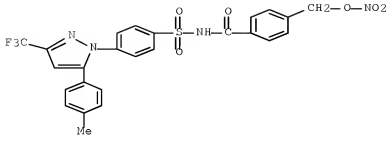
II

AB Novel compds. of formulas I and II [R = H, alkyl; L = bond, alkylidene, cycloalkylidene, aryl, etc.; X = O, S; Y = bond, S, O, (substituted) NH; m = 0-4; n = 1-2; p = 1-4] are prepared, which are nitric oxide-releasing prodrugs useful in the treatment of cyclooxygenase-2 mediated diseases. The invention also encompasses certain pharmaceutical compns. and methods for treatment of cyclooxygenase-2 mediated diseases comprising the use of compds. I or II. The above compds. may be used as a combination therapy with low-dose aspirin to treat chronic cyclooxygenase-2 mediated diseases or conditions while simultaneously reducing the risk of thrombotic cardiovascular events.

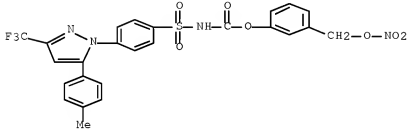
IT 586347-24-2P 685106-98-3P 685107-04-4P
685107-08-8P 685107-12-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of nitrosated or nitrosylated prodrugs for cyclooxygenase-2 inhibitors)

RN 586347-24-2 ZCAPLUS

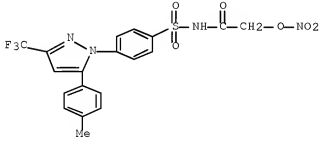
CN Benzamide, N-[[4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]phenyl]sulfonyl]-4-[(nitrooxy)methyl]- (CA INDEX NAME)



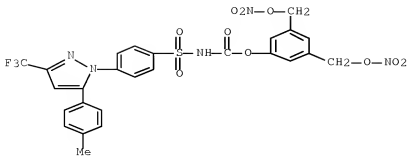
RN 685106-98-3 ZCAPLUS
CN Carbamic acid, [[4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]phenyl]sulfonyl]-, 3-[(nitrooxy)methyl]phenyl ester (9CI) (CA INDEX NAME)



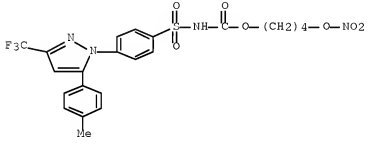
RN 685107-04-4 ZCAPLUS
CN Acetamide, N-[[4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]phenyl]sulfonyl]-2-(nitrooxy)- (CA INDEX NAME)



RN 685107-08-8 ZCAPLUS
CN Carbamic acid, [[4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]phenyl]sulfonyl]-, 3,5-bis[(nitrooxy)methyl]phenyl ester (9CI) (CA INDEX NAME)



RN 685107-12-4 ZCAPLUS
CN Carbamic acid, [[4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]phenyl]sulfonyl]-, 4-(nitrooxy)butyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 4 OF 5 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:2830 ZCAPLUS Full-text
DOCUMENT NUMBER: 140:59410
TITLE: Preparation of nitrooxy derivatives of cyclooxygenase-2 inhibitors
INVENTOR(S): Del Soldato, Piero; Santus, Giancarlo
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000781	A2	20031231	WO 2003-EP6502	20030620
WO 2004000781	A3	20041014		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

IT	2002MI1391	A1	20031229	IT 2002-MI1391		20020625
CA	2491209	A1	20031231	CA 2003-2491209		20030620
AU	2003245972	A1	20040106	AU 2003-245972		20030620
EP	1517889	A2	20050330	EP 2003-738069		20030620
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
CN	1662490	A	20050831	CN 2003-814682		20030620
JP	2005530836	T	20051013	JP 2004-514803		20030620
NZ	537043	A	20060929	NZ 2003-537043		20030620
RU	2339617	C2	20081127	RU 2004-138552		20030620
ZA	2004010060	A	20051020	ZA 2004-10060		20041213
MX	2004012851	A	20050224	MX 2004-12851		20041216
US	20060106082	A1	20060518	US 2005-516938		20050913
PRIORITY APPLN. INFO.:				IT 2002-MI1391	A	20020625
				WO 2003-EP6502	W	20030620

OTHER SOURCE(S): MARPAT 140:59410

AB Disclosed are new compds. able to release COX-2 inhibitors and NO (no data) having formula M-T-YA-NO2 [wherein M-T = the residue of a COX-2 selective inhibitor (T = SO2NH, SO2NR, CO, O, S, NH, N(SO2R); R = C1-10 alkyl; the COX-2 selective inhibitor, M-TH or M-TOH, has to meet test 2 mentioned in the description); YA = -(B)b0-(C)c0- [b0, c0 = 0,1, with the proviso that b0 and c0 cannot be simultaneously 0; B = TB-X2-TB1; TB = CO, X; X = O, S, NH, NR, R (defined above); TB = CO when T = SO2NH, SO2NR-O, S, NH, or N(SO2R), TB = X when T = CO; TB1 = CO or X (defined above); X2 = a divalent radical selected from the following compds. Q or Q1, etc. (n1, n2 = 0, 1; R2, R3 = H, Me; Y1 = CH2CH2, CH:CH(CH2)n2; n2 = 0, 1)]] for the treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, Alzheimer's disease, or disorders resulting from elevated levels of COX-2. These compds. including 5-niroxypentanoc acid, 4-nitrooxybutyric acid, and 4-nitrooxybutyramide, 2-nitroxymethylbenzoic acid ester derivs. mitigate or remove the known side-effects of COX-2 inhibitors. The inflammatory disorders are selected from the group consisting of, but not limited to, arthritis, rheumatoid arthritis, osteoarthritis, allergic rhinitis, sinusitis, chronic obstructive pulmonary diseases, dermatitis, psoriasis, cystic fibrosis, multiple sclerosis, vasculitis and organ transplant rejection. The cardiovascular diseases are selected from the group consisting of, but not limited to, atherosclerosis, restenosis, coronary artery disease, angina, diabetes mellitus, diabetic nephropathy, diabetic retinopathy, stroke and myocardial infarct. The gastrointestinal disorders are selected from the group consisting of, but not limited to, inflammatory intestinal disorders, Crohn's disease, gastritis, ulcerative colitis, peptic ulcer, hemorrhagic ulcer, gastric hyperacidity, dyspepsia, gastroparesis, Zollinger-Ellison's syndrome, bacterial infections, hypersecretory states associated with systemic mastocytosis or basophilic leukemia and hyperhystaminemia. The disorders resulting from elevated levels of COX-2 are selected from the group consisting of, but not limited to, angiogenesis, arthritis, asthma, bronchitis, menstrual cramps, tendonitis, bursitis, neoplasia, ophthalmic diseases, pulmonary inflammations, central nervous system disorders, allergic rhinitis, atherosclerosis, endothelial disorders, organs and tissues preservation, inhibition and/or prevention of platelets aggregation. Thus, N-[6-[(2,4-difluorophenyl)thio]-2,3-dihydro-1-oxo-1-inden-5-yl]-N-[4- (chloro)butyroyloxymethyl]methanesulfonamide. A solution of chloromethyl (4-chloro)butyrate (1 g, 5.40 mmol) in anhydrous THF (5 mL) was slowly added dropwise in a suspension of N-[6-[(2,4-difluorophenyl)thio]-2,3-dihydro-1- oxo-1-inden-5-yl]methanesulfonamide sodium salt (2.04 g, 5.40 mmol) in anhydrous THF (25 mL) and stirred at room temperature overnight to give,

after workup and silica gel chromatog., N-[6-[(2,4-difluorophenyl)thio]-2,3-dihydro-1-oxo-1-inden-5-yl]-N-[4-(chloro)butyroyloxymethyl]methanesulfonamide (I). A solution of I (1 g, 1.98 mmol) in MeCN (20 mL) was added with AgNO3 (0.67 g, 3.96 mmol), heated at 80° for 15 h in the absence of light, filtered to remove the silver salt, evaporated under vacuum, and purified by chromatog. on a silica gel column to give with n-hexane/ethyl acetate 8/2 as eluent to give 503 mg N-[6-[(2,4-difluorophenyl)thio]-2,3-dihydro-1-oxo-1-inden-5-yl]-N-[4-(nitrooxy)butyroyloxymethyl]methanesulfonamide.

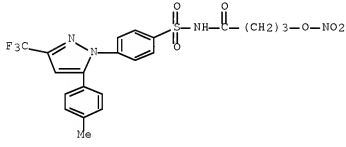
IT 586347-45-7P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)

RN 586347-45-7 ZCAPLUS

CN Butanamide, N-[[4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]phenyl]sulfonyl]-4-(nitrooxy)- (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 5 OF 5 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:652131 ZCAPLUS Full-text

DOCUMENT NUMBER: 139:214237

TITLE: Preparation of nitrate prodrugs able to release nitric oxide in a controlled and selective way and their use for prevention and treatment of inflammatory, ischemic and proliferative diseases

INVENTOR(S): Scaramuzzino, Giovanni

PATENT ASSIGNEE(S): Italy

SOURCE: Eur. Pat. Appl., 313 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1336602	A1	20030820	EP 2002-425075	20020213
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: EP 2002-425075 20020213

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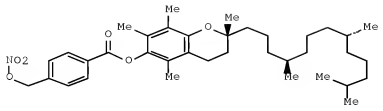


II

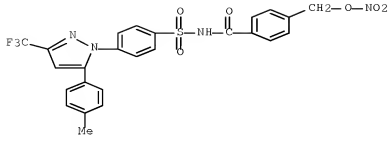
AB New pharmaceutical compds. of general formula F-(X)q (I) [q = 1-5, preferably 1; F is chosen among drugs such as δ-tocopherol, clidanac, diethylhomospermine, glucosamine, thymocartin, vofopitant, etc.; X is chosen among 4 groups M, T, V, and Y where M = ONO2, nitrate salt, nitrite ester, ONO, thoinitrite, SNO, etc., T = OR1-M, OR1OR1-M, SR1NR2R1-M, NR2R1-M, NR2R1SR1-M, etc., R1 = saturated or unsatd., linear or branched alkylene, having 1 to 21 carbon atoms or a saturated or unsatd., optionally heterosubstituted or branched cycloalkylene, having 3 to 7 carbon atoms or an optionally heterosubstituted arylene having 3 to 7 carbon atoms; R2 = H, saturated or unsatd., linear or branched 1-21 carbon atom alkyl, saturated or unsatd. optionally heterosubstituted or branched 3-7 carbon cycloalkyl, optionally heterosubstituted 3-7 carbon aryl; R1, R2 = OH, SH, F, Cl, Br, OPO3H2, CO2H, etc.; bond between F and T = carboxylic ester, carboxylic amide, glycoside, azo, thioester, sulfonic ester, etc.; V = Z-M2, OZ-M2, NR2Z-M2, R1Z-M2, OR1-M2, OR1Z-M2, M2 = M, R1-M, OR1-M, SR1-M, NR2R1-M; ZM2 = COCH2CH(M2)CH2N+Me3, COCH2CH2COM2, COCH(NHR2)CH2M2, etc.; Y = 4-COC6H4CH2ONO2, O(CH2)4ONO2, COCH(NH2)CH2ONO2, 3-OC6H4CH2ONO2, etc.] were prepared For example, α-tocopherol reacted with 4-HO2CC6H4CH2ONO2 to give the nitroxymethyl derivative II. The compds. of general formula I are nitrate prodrugs which can release nitric oxide in vivo in a controlled and selective way and without hypotensive side effects and for this reason they are useful for the preparation of medicines for prevention and treatment of inflammatory, ischemic, degenerative and proliferative diseases of musculoskeletal, tegumental, respiratory, gastrointestinal, genito-urinary and central nervous systems.

IT 586347-24-2P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

RN 586347-24-2 ZCAPLUS

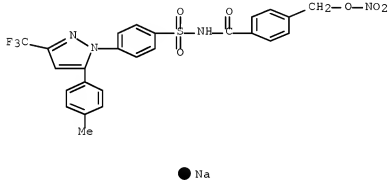
CN Benzamide, N-[[4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]phenyl]sulfonyl]-4-[(nitrooxy)methyl]- (CA INDEX NAME)



IT 586347-25-3P 586347-45-7P 586347-46-8P
586347-47-9P 586347-62-8P 586347-63-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

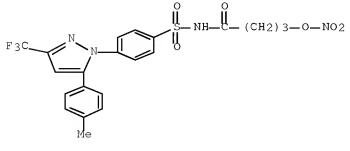
RN 586347-25-3 ZCAPLUS

CN Benzamide, N-[[4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]phenyl]sulfonyl]-4-[(nitrooxy)methyl]-, sodium salt (1:1) (CA INDEX NAME)

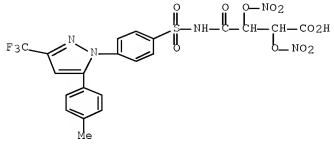


RN 586347-45-7 ZCAPLUS

CN Butanamide, N-[[4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]phenyl]sulfonyl]-4-(nitrooxy)- (CA INDEX NAME)

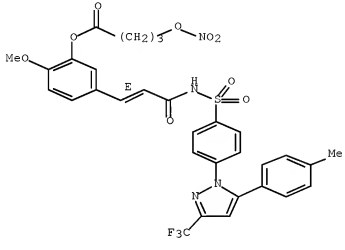


RN 586347-46-8 ZCAPLUS
CN Butanoic acid, 4-[[[4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]phenyl]sulfonyl]amino]-2,3-bis(nitrooxy)-4-oxo- (CA INDEX NAME)

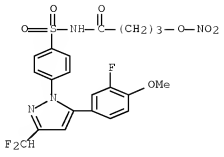


RN 586347-47-9 ZCAPLUS
CN Butanoic acid, 4-(nitrooxy)-, 2-methoxy-5-[(1E)-3-[[[4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]phenyl]sulfonyl]amino]-3-oxo-1-propen-1-yl]phenyl ester (CA INDEX NAME)

Double bond geometry as shown.

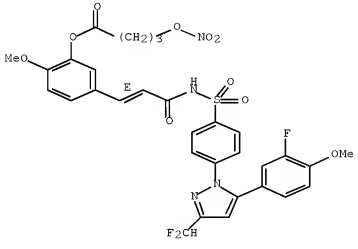


RN 586347-62-8 ZCAPLUS
CN Butanamide, N-[[4-[3-(difluoromethyl)-5-(3-fluoro-4-methoxyphenyl)-1H-pyrazol-1-yl]phenyl]sulfonyl]-4-(nitrooxy)- (CA INDEX NAME)



RN 586347-63-9 ZCAPLUS
CN Butanoic acid, 4-(nitrooxy)-, 5-[(1E)-3-[[[4-[3-(difluoromethyl)-5-(3-fluoro-4-methoxyphenyl)-1H-pyrazol-1-yl]phenyl]sulfonyl]amino]-3-oxo-1-propen-1-yl]-2-methoxyphenyl ester (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> file registry
FILE 'REGISTRY' ENTERED AT 15:09:15 ON 07 MAY 2009
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provided by InfoChem.

STRUCTURE FILE UPDATES:    6 MAY 2009  HIGHEST RN 1143575-54-5
DICTIONARY FILE UPDATES:   6 MAY 2009  HIGHEST RN 1143575-54-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 9, 2009.

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
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experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

Uploading L3b.str
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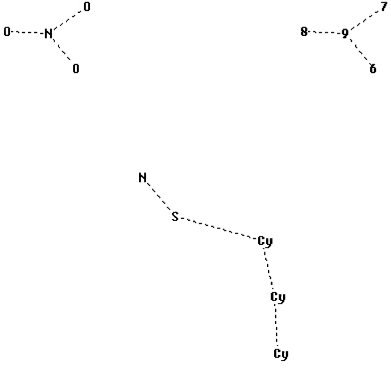


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chain nodes :
1  2  3  4  5  6  7  8  9
chain bonds :
1-2  1-3  3-4  4-5  6-9  7-9  8-9
exact/norm bonds :
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1-2 1-3 3-4 4-5 6-9 7-9 8-9

Connectivity :
2:2 M minimum RC ring/chain
Match level :
1:CLASS 2:CLASS 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:CLASS

=> file zcaplus
FILE 'ZCAPLUS' ENTERED AT 15:09:18 ON 07 MAY 2009
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 7 May 2009 VOL 150 ISS 19
FILE LAST UPDATED: 6 May 2009 (20090506/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2009

ZCAplus now includes complete International Patent Classification (IPC)
reclassification data for the third quarter of 2008.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate
substance identification.
'OBI' IS DEFAULT SEARCH FIELD FOR 'ZCAPLUS' FILE

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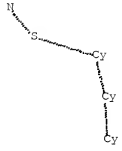
L3 STR

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L6             6 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  L5


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FILE 'BEILSTEIN' ENTERED AT 15:09:26 ON 07 MAY 2009
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FILE LAST UPDATED ON April 1, 2008

FILE COVERS 1771 TO 2008.
*** FILE CONTAINS 10.322,808  SUBSTANCES ***

>>>PLEASE NOTE: Reaction Data and substance data are stored in
   separate documents and can not be searched together in one query.
   Reaction data for BEILSTEIN compounds may be displayed
   immediately with the display codes PRE (preparations) and REA
   (reactions).  A substance answer set retrieved after the search
   for a chemical name, a compounds with available reaction
   information by combining with PRE/FA, REA/FA or more generally
   with RX/FA. The BEILSTEIN Registry Number (BRN) is the link
   between a BEILSTEIN compound and belonging reactions. For mo
   detailed reaction searches BRNs can be searched as reaction
   partner BRNs Reactant BRN (RX.RBRN) or Product BRN (RX.PBRN).<<<

>>> FOR SEARCHING PREPARATIONS SEE HELP PRE  <<<

**********************************************************************
* PLEASE NOTE THAT THERE ARE NO FORMATS FREE OF COST.                *
* SET NOTICE FEATURE: THE COST ESTIMATES CALCULATED FOR SET NOTICE   *
* ARE BASED ON THE HIGHEST PRICE CATEGORY. THEREFORE; THESE          *
* ESTIMATES MAY NOT REFLECT THE ACTUAL COSTS.                        *
* FOR PRICE INFORMATION SEE HELP COST                                *
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>>> Price change as of January 1st, 2008: Connect Time and Structure
    Search fees re-introduced. See NEWS and HELP COST <<<

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L3              STR
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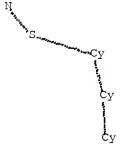


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Structure attributes must be viewed using STN Express query preparation.
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100.0% PROCESSED     101 ITERATIONS                              0 ANSWERS
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FILW IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> file wpix
FILE 'WPIX' ENTERED AT 15:09:37 ON 07 MAY 2009
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FILE LAST UPDATED:          7 MAY 2009   <20090507/UP>
MOST RECENT UPDATE:           200928      <200928/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE
>>> Now containing more than 1.3 million chemical structures in DCR <<<

>>> IPC, ECLA and US National Classifications  have been updated
    with reclassifications to March 15th,  2009.
    F-Term and FI-Term original classifications are current and
    reclassification will commence in June.
    No update date (UP) has been created for the reclassified
    documents, but they can be identified by
    specific update codes (see HELP CLA for details)<<<
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FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
PLEASE VISIT:
http://www.stn-international.com/stn_guide.html

FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://scientific.thomsonreuters.com/support/patents/coverage/latestupdates/

EXPLORE DERWENT WORLD PATENTS INDEX IN STN ANAVIST, VERSION 2.0:
http://www.stn-international.com/DWPIAnaVist2_0608.html

>>> HELP for European Patent Classifications see HELP ECLA, HELP ICO <<<

'BIX' IS DEFAULT SEARCH FIELD FOR 'WPIX' FILE

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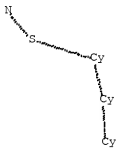
L3 STR



Structure attributes must be viewed using STN Express query preparation.
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L11 5 SEA FILE=WPIX SPE=ON ABB=ON PLU=ON L10/DCR

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ENTER REMOVE, IDENTIFY, ONLY, OR (?):end

=> dup rem L6 L8 L11
L8 HAS NO ANSWERS
DUPLICATE IS NOT AVAILABLE IN 'BEILSTEIN'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
FILE 'ZCAPLUS' ENTERED AT 15:10:02 ON 07 MAY 2009
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE 'WPIX' ENTERED AT 15:10:02 ON 07 MAY 2009

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PROCESSING COMPLETED FOR L6
PROCESSING COMPLETED FOR L8
PROCESSING COMPLETED FOR L11
L32             6 DUP REM L6 L8 L11 (5 DUPLICATES REMOVED)
                  ANSWERS '1-6' FROM FILE ZCAPLUS

=> d ibib abs hitstr L32 1-6

L32  ANSWER 1 OF 6  ZCAPLUS  COPYRIGHT 2009 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2006:191976  ZCAPLUS  Full-text
DOCUMENT NUMBER:          144:273755
TITLE:                    Preparation of prodrugs containing novel biocleavable
                          linkers
INVENTOR(S):              Satyam, Apparao
PATENT ASSIGNEE(S):       Nicholas Piramal India Ltd., India
SOURCE:                   U.S. Pat. Appl. Publ., 181 pp.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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     US 20060046967       A1    20060302    US 2005-213396         20050826
     US 20060205674       A2    20060914
     AU 2005281359        A1    20060316    AU 2005-281359         20050826
     CA 2577490           A1    20060316    CA 2005-2577490        20050826
     WO 2006027711        A2    20060316    WO 2005-IB52797        20050826
     WO 2006027711        A3    20070315
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             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
             LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
             NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
             SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
             ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
     EP 1789091           A2    20070530    EP 2005-781464         20050826
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             BA, HR, MK, YU
     CN 101039701         A     20070919    CN 2005-80034555       20050826
     JP 2008510795        T     20080410    JP 2007-529100         20050826
     BR 2005015218        A     20080708    BR 2005-15218          20050826
     KR 2007053214        A     20070523    KR 2007-702931         20070206
     MX 2007002210        A     20070507    MX 2007-2210           20070223
     IN 2007MN00439       A     20070720    IN 2007-MN439          20070326
PRIORITY APPLN. INFO.:                       US 2004-604632P     P  20040826
                                             IN 2005-MU779       A  20050701
                                             WO 2005-IB52797     W  20050826
OTHER SOURCE(S):          CASREACT 144:273755; MARPAT 144:273755
AB   The invention provides compds. D1-L1-E-A-B-A1-E-(L-E-A1-B-A-E)0-2-L2-D2 [B is
     a bond, (CH2)1-6, (CH2CH2O)1-1000, S-S, S-S:O, S-SO2 or S-S:NH; A, A1 are
     independently a bond, (CH2)1-8, 1,2-, 1,3- or 1,4-phenylene; D1 is a
```
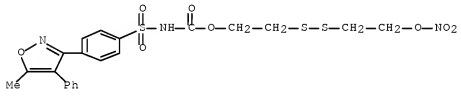
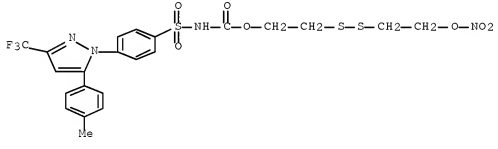

therapeutic agent having one or more functional groups OH, SH, NHR1, CO2H, CONHR1, O2CNHR1, SO2NHR1, SO2NHR1, NR1CONHNHR1 or NR1SO2NHR1 (R1 is H, alkyl, aryl, etc.); D2 is D1, a peptide, protein, monoclonal antibody, vitamin, NO, NO2, NONOate, a nitric oxide-releasing group, a polymer, etc.; E is independently CH2 or a bond; L1, L2 are independently a bond, O, S, NR1, L, or a linkage] or their pharmaceutically-acceptable salts for use as prodrugs, including NO-releasing prodrugs. Thus, aspirin prodrug 2-AcOC6H4CONHCH2CH2SSCH2CH2ONO2 was prepared and shown to release salicylate in rats in a sustained and controlled manner starting from 1 h through 12 h.

IT 877865-24-2P 877865-25-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of prodrugs containing novel biocleavable linkers)

RN 877865-24-2 ZCAPLUS
CN Carbamic acid, [[4-(5-methyl-4-phenyl-3-isoxazolyl)phenyl]sulfonyl]-, 2-[[2-(nitrooxy)ethyl]dithio]ethyl ester (9CI) (CA INDEX NAME)



RN 877865-25-3 ZCAPLUS
CN Carbamic acid, [[4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]phenyl]sulfonyl]-, 2-[[2-(nitrooxy)ethyl]dithio]ethyl ester (9CI) (CA INDEX NAME)



L32 ANSWER 2 OF 6 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 2

ACCESSION NUMBER:	2005:547257 ZCAPLUS Full-text
DOCUMENT NUMBER:	143:77866
TITLE:	Preparation of nitrate esters having a β- or γ-sulfur atom for protection of cells/tissues from oxidative damage.
INVENTOR(S):	Thatcher, Gregory R. j.; Bennett, Brian M.; Reynolds, James N.; Boegman, Roland J.; Jhamandas, Khem
PATENT ASSIGNEE(S):	USA
SOURCE:	U.S. Pat. Appl. Publ., 83 pp., Cont.-in-part of U.S.

Ser. No. 147,808.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20050137191	A1	20050623	US 2004-943264	20040917
US 5807847	A	19980915	US 1996-658145	19960604
US 5883122	A	19990316	US 1997-867856	19970603
US 6310052	B1	20011030	US 1999-267379	19990315
US 7115661	B1	20061003	US 1999-473713	19991229
EP 1518553	A2	20050330	EP 2004-28372	20001227
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
US 20020177622	A1	20021128	US 2002-147808	20020520
US 6916835	B2	20050712		
AU 2005284573	A1	20060323	AU 2005-284573	20050916
CA 2580627	A1	20060323	CA 2005-2580627	20050916
WO 2006029532	A1	20060323	WO 2005-CA1417	20050916
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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1797100	A1	20070620	EP 2005-787832	20050916
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				

PRIORITY APPLN. INFO.:

US 1996-658145	A2 19960604
US 1997-867856	A2 19970603
US 1999-267379	A3 19990315
US 1999-473713	A2 19991229
US 2002-147808	A2 20020520
EP 2000-986925	A3 20001227
US 2001-851591	A3 20010510
US 2002-108513	A3 20020329
US 2004-943264	A 20040917
WO 2005-CA1417	W 20050916

OTHER SOURCE(S): CASREACT 143:77866; MARPAT 143:77866

AB YXCR3R4(CR17R18)n(CR1R2)mONO2 [m, n = 0-10; R3, R4, R17 = H, nitrate, A; R1 = H, A; A = (substituted) (unsatd.) (cyclic) aliphatyl; R1R3, R4R17 = aliphatyl linkage; R2, R18 = H, A, XY; X = F, Cl, Br, Cl, NO2, CH2, CF2, O, NH, NMe, cyano, NHOH, N3, S, SCN, SO, SO2, etc.; Y = null, F, Cl, Br, Cl, Me, CF2H, CF3, OH, NH2, S, SCN, SH, etc.; with provisos], were prepared Thus, [O2NOCH2CH(ONO2)CH2S]2 (prepared via the corresponding Bunte salt) at 200 μmol/kg s.c. gave virtually complete protection against 6-OHDA killing of dopaminergic neurons in rats.

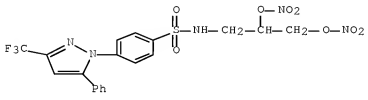
IT 854925-45-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(claimed compound; preparation of nitrate esters having β- or γ-sulfur atom for protection of cells/tissues from oxidative damage)

RN 854925-45-4 ZCAPLUS

CN Benzenesulfonamide, N-[2,3-bis(nitrooxy)propyl]-4-[5-phenyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (CA INDEX NAME)



L32 ANSWER 3 OF 6 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 2004:370913 ZCAPLUS Full-text

DOCUMENT NUMBER: 140:375166

TITLE: Preparation of nitric oxide releasing selective cyclooxygenase-2 inhibitors

INVENTOR(S): Wang, Zhaoyin; Young, Robert N.; Zamboni, Robert

PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.

SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004037798	A1	20040506	WO 2003-CA1605	20031021
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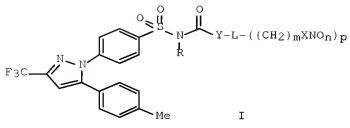
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2503063	A1	20040506	CA 2003-2503063	20031021
AU 2003278039	A1	20040513	AU 2003-278039	20031021
EP 1562914	A1	20050817	EP 2003-769122	20031021
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 20060058363	A1	20060316	US 2005-530214	20050404

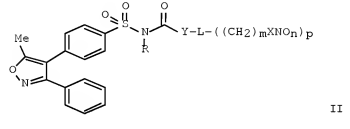
PRIORITY APPLN. INFO.: US 2002-420292P P 20021022
WO 2003-CA1605 W 20031021

OTHER SOURCE(S): MARPAT 140:375166

GI



I



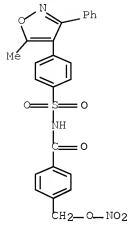
II

AB Novel compds. of formulas I and II [R = H, alkyl; L = bond, alkylidene, cycloalkylidene, aryl, etc.; X = O, S; Y = bond, S, O, (substituted) NH; m = 0-4; n = 1-2; p = 1-4] are prepared, which are nitric oxide-releasing prodrugs useful in the treatment of cyclooxygenase-2 mediated diseases. The invention also encompasses certain pharmaceutical compns. and methods for treatment of cyclooxygenase-2 mediated diseases comprising the use of compds. I or II. The above compds. may be used as a combination therapy with low-dose aspirin to treat chronic cyclooxygenase-2 mediated diseases or conditions while simultaneously reducing the risk of thrombotic cardiovascular events.

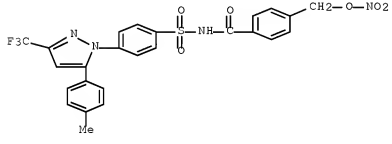
IT 586347-22-0P 586347-24-2P 685106-98-3P
685107-00-0P 685107-04-4P 685107-06-6P
685107-08-8P 685107-10-2P 685107-12-4P
685107-14-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of nitrosated or nitrosylated prodrugs for cyclooxygenase-2 inhibitors)

RN 586347-22-0 ZCAPLUS

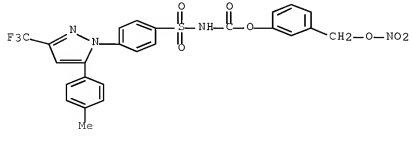
CN Benzamide, N-[[4-(5-methyl-3-phenyl-4-isoxazolyl)phenyl]sulfonyl]-4-[(nitrooxy)methyl]- (CA INDEX NAME)



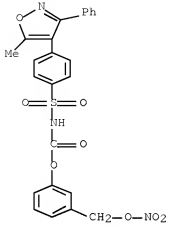
RN 586347-24-2 ZCAPLUS
CN Benzamide, N-[[4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]phenyl]sulfonyl]-4-[(nitrooxy)methyl]- (CA INDEX NAME)



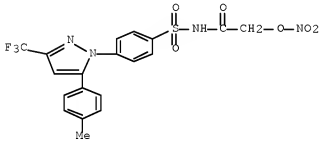
RN 685106-98-3 ZCAPLUS
CN Carbamic acid, [[4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]phenyl]sulfonyl]-, 3-[(nitrooxy)methyl]phenyl ester (9CI) (CA INDEX NAME)



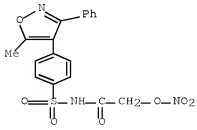
RN 685107-00-0 ZCAPLUS
CN Carbamic acid, [[4-(5-methyl-3-phenyl-4-isoxazolyl)phenyl]sulfonyl]-, 3-[(nitrooxy)methyl]phenyl ester (9CI) (CA INDEX NAME)



RN 685107-04-4 ZCAPLUS
CN Acetamide, N-[[4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]phenyl]sulfonyl]-2-(nitrooxy)- (CA INDEX NAME)

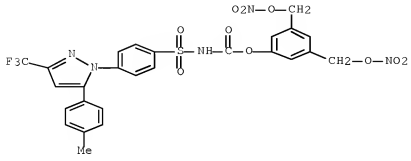


RN 685107-06-6 ZCAPLUS
CN Acetamide, N-[[4-(5-methyl-3-phenyl-4-isoxazolyl)phenyl]sulfonyl]-2-(nitrooxy)- (CA INDEX NAME)

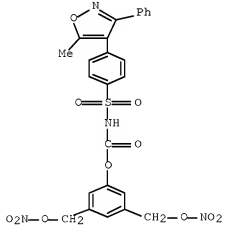


RN 685107-08-8 ZCAPLUS
CN Carbamic acid, [[4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-

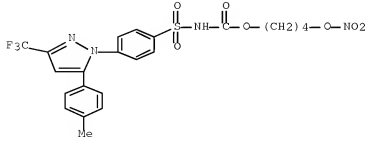
yl]phenyl]sulfonyl]-, 3,5-bis[(nitrooxy)methyl]phenyl ester (9CI) (CA INDEX NAME)



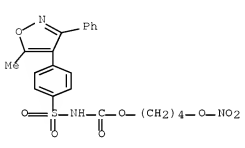
RN 685107-10-2 ZCAPLUS
CN Carbamic acid, [[4-(5-methyl-3-phenyl-4-isoxazolyl)phenyl]sulfonyl]-, 3,5-bis[(nitrooxy)methyl]phenyl ester (9CI) (CA INDEX NAME)



RN 685107-12-4 ZCAPLUS
CN Carbamic acid, [[4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]phenyl]sulfonyl]-, 4-(nitrooxy)butyl ester (9CI) (CA INDEX NAME)



RN 685107-14-6 ZCAPLUS
CN Carbamic acid, [[4-(5-methyl-3-phenyl-4-isoxazolyl)phenyl]sulfonyl]-, 4-(nitrooxy)butyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 4 OF 6 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2004:2830 ZCAPLUS Full-text
DOCUMENT NUMBER: 140:59410
TITLE: Preparation of nitrooxy derivatives of cyclooxygenase-2 inhibitors
INVENTOR(S): Del Soldato, Piero; Santus, Giancarlo
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000781	A2	20031231	WO 2003-EP6502	20030620
WO 2004000781	A3	20041014		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IT 2002MI1391	A1	20031229	IT 2002-MI1391	20020625
CA 2491209	A1	20031231	CA 2003-2491209	20030620
AU 2003245972	A1	20040106	AU 2003-245972	20030620
EP 1517889	A2	20050330	EP 2003-738069	20030620
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1662490	A	20050831	CN 2003-814682	20030620
JP 2005530836	T	20051013	JP 2004-514803	20030620
NZ 537043	A	20060929	NZ 2003-537043	20030620

RU 2339617	C2	20081127	RU 2004-138552		20030620
ZA 2004010060	A	20051020	ZA 2004-10060		20041213
MX 2004012851	A	20050224	MX 2004-12851		20041216
US 20060106082	A1	20060518	US 2005-516938		20050913
PRIORITY APPLN. INFO.:			IT 2002-MI1391	A	20020625
			WO 2003-EP6502	W	20030620

OTHER SOURCE(S): MARPAT 140:59410

AB Disclosed are new compds. able to release COX-2 inhibitors and NO (no data) having formula M-T-YA-NO2 [wherein M-T = the residue of a COX-2 selective inhibitor (T = SO2NH, SO2NR, CO, O, S, NH, N(SO2R); R = C1-10 alkyl; the COX-2 selective inhibitor, M-TH or M-TOH, has to meet test 2 mentioned in the description); YA = -(B)b0-(C)c0- [b0, c0 = 0,1, with the proviso that b0 and c0 cannot be simultaneously 0; B = TB-X2-TB1; TB = CO, X; X = O, S, NH, NR, R (defined above); TB = CO when T = SO2NH, SO2NR-O, S, NH, or N(SO2R), TB = X when T = CO; TB1 = CO or X (defined above); X2 = a divalent radical selected from the following compds. Q or Q1, etc. (n1, n2 = 0, 1; R2, R3 = H, Me; Y1 = CH2CH2, CH:CH(CH2)n2; n2 = 0, 1)]] for the treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, Alzheimer's disease, or disorders resulting from elevated levels of COX-2. These compds. including 5-niroxypentanoc acid, 4-nitrooxybutyric acid, and 4-nitrooxybutyramide, 2-nitroxymethylbenzoic acid ester derivs. mitigate or remove the known side-effects of COX-2 inhibitors. The inflammatory disorders are selected from the group consisting of, but not limited to, arthritis, rheumatoid arthritis, osteoarthritis, allergic rhinitis, sinusitis, chronic obstructive pulmonary diseases, dermatitis, psoriasis, cystic fibrosis, multiple sclerosis, vasculitis and organ transplant rejection. The cardiovascular diseases are selected from the group consisting of, but not limited to, atherosclerosis, restenosis, coronary artery disease, angina, diabetes mellitus, diabetic nephropathy, diabetic retinopathy, stroke and myocardial infarct. The gastrointestinal disorders are selected from the group consisting of, but not limited to, inflammatory intestinal disorders, Crohn's disease, gastritis, ulcerative colitis, peptic ulcer, hemorrhagic ulcer, gastric hyperacidity, dyspepsia, gastroparesis, Zollinger-Ellison's syndrome, bacterial infections, hypersecretory states associated with systemic mastocytosis or basophilic leukemia and hyperhystaminemia. The disorders resulting from elevated levels of COX-2 are selected from the group consisting of, but not limited to, angiogenesis, arthritis, asthma, bronchitis, menstrual cramps, tendonitis, bursitis, neoplasia, ophthalmic diseases, pulmonary inflammations, central nervous system disorders, allergic rhinitis, atherosclerosis, endothelial disorders, organs and tissues preservation, inhibition and/or prevention of platelets aggregation. Thus, N-[6-[(2,4-difluorophenyl)thio]-2,3-dihydro-1-oxo-1-inden-5-yl]-N-[4- (chloro)butyroyloxymethyl]methanesulfonamide. A solution of chloromethyl (4-chloro)butyrate (1 g, 5.40 mmol) in anhydrous THF (5 mL) was slowly added dropwise in a suspension of N-[6-[(2,4-difluorophenyl)thio]-2,3-dihydro-1- oxo-1-inden-5-yl]methanesulfonamide sodium salt (2.04 g, 5.40 mmol) in anhydrous THF (25 mL) and stirred at room temperature overnight to give, after workup and silica gel chromatog., N-[6-[(2,4-difluorophenyl)thio]-2,3-dihydro-1-oxo-1-inden-5-yl]-N-[4-(chloro)butyroyloxymethyl]methanesulfonamide (I). A solution of I (1 g, 1.98 mmol) in MeCN (20 mL) was added with AgNO3 (0.67 g, 3.96 mmol), heated at 80° for 15 h in the absence of light, filtered to remove the silver salt, evaporated under vacuum, and purified by chromatog. on a silica gel column to give with n-hexane/ethyl acetate 8/2 as eluent to give 503 mg N-[6-[(2,4-difluorophenyl)thio]-2,3-dihydro-1-oxo-1-inden-5-yl]-N-[4-(nitrooxy)butyroyloxymethyl]methanesulfonamide.

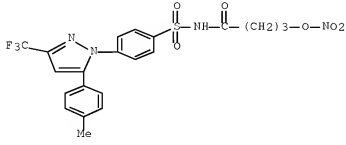
IT 586347-45-7P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)

RN 586347-45-7 ZCAPLUS

CN Butanamide, N-[[4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]phenyl]sulfonyl]-4-(nitrooxy)- (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 5 OF 6 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 5

ACCESSION NUMBER: 2003:652131 ZCAPLUS Full-text

DOCUMENT NUMBER: 139:214237

TITLE: Preparation of nitrate prodrugs able to release nitric oxide in a controlled and selective way and their use for prevention and treatment of inflammatory, ischemic and proliferative diseases

INVENTOR(S): Scaramuzzino, Giovanni

PATENT ASSIGNEE(S): Italy

SOURCE: Eur. Pat. Appl., 313 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

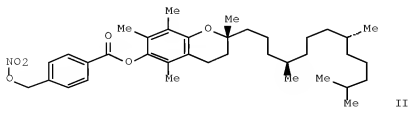
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1336602	A1	20030820	EP 2002-425075	20020213
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRIORITY APPLN. INFO.:			EP 2002-425075	20020213

GI



II

AB New pharmaceutical compds. of general formula F-(X)q (I) [q = 1-5, preferably 1; F is chosen among drugs such as δ-tocopherol, clidanac, diethylhomospermine, glucosamine, thymocartin, vofopitant, etc.; X is chosen among 4 groups M, T, V, and Y where M = ONO2, nitrate salt, nitrite ester, ONO, thoinitrite, SNO, etc., T = OR1-M, OR1OR1-M, SR1NR2R1-M, NR2R1-M, NR2R1SR1-M, etc., R1 = saturated or unsatd., linear or branched alkylene, having 1 to 21 carbon atoms or a saturated or unsatd., optionally heterosubstituted or branched cycloalkylene, having 3 to 7 carbon atoms or an optionally heterosubstituted arylene having 3 to 7 carbon atoms; R2 = H, saturated or unsatd., linear or branched 1-21 carbon atom alkyl, saturated or unsatd. optionally heterosubstituted or branched 3-7 carbon cycloalkyl, optionally heterosubstituted 3-7 carbon aryl; R1, R2 = OH, SH, F, Cl, Br, OPO3H2, CO2H, etc.; bond between F and T = carboxylic ester, carboxylic amide, glycoside, azo, thioester, sulfonic ester, etc.; V = Z-M2, OZ-M2, NR2Z-M2, R1Z-M2, OR1-M2, OR1Z-M2, M2 = M, R1-M, OR1-M, SR1-M, NR2R1-M; ZM2 = COCH2CH(M2)CH2N+Me3, COCH2CH2COM2, COCH(NHR2)CH2M2, etc.; Y = 4-COC6H4CH2ONO2, O(CH2)4ONO2, COCH(NH2)CH2ONO2, 3-OC6H4CH2ONO2, etc.] were prepared For example, α-tocopherol reacted with 4-HO2CC6H4CH2ONO2 to give the nitroxymethyl derivative II. The compds. of general formula I are nitrate prodrugs which can release nitric oxide in vivo in a controlled and selective way and without hypotensive side effects and for this reason they are useful for the preparation of medicines for prevention and treatment of inflammatory, ischemic, degenerative and proliferative diseases of musculoskeletal, tegumental, respiratory, gastrointestinal, genito-urinary and central nervous systems.

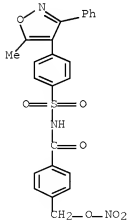
IT 586347-22-0P

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

RN 586347-22-0 ZCAPLUS

CN Benzamide, N-[[4-(5-methyl-3-phenyl-4-isoxazolyl)phenyl]sulfonyl]-4-[(nitrooxy)methyl]- (CA INDEX NAME)

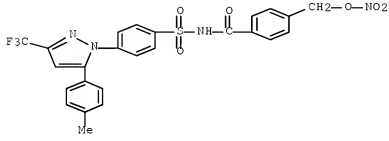


IT 586347-24-2P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

RN 586347-24-2 ZCAPLUS

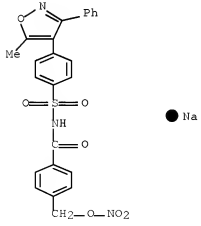
CN Benzamide, N-[[4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]phenyl]sulfonyl]-4-[(nitrooxy)methyl]- (CA INDEX NAME)



IT 586347-23-1P 586347-25-3P 586347-39-9P
586347-45-7P 586347-46-8P 586347-47-9P
586347-48-0P 586347-50-4P 586347-57-1P
586347-62-8P 586347-63-9P 586347-65-1P
586347-66-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

RN 586347-23-1 ZCAPLUS

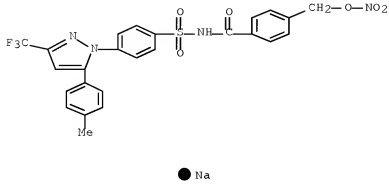
CN Benzamide, N-[[4-(5-methyl-3-phenyl-4-isoxazolyl)phenyl]sulfonyl]-4-[(nitrooxy)methyl]-, sodium salt (1:1) (CA INDEX NAME)



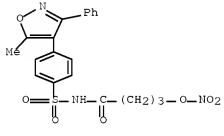
RN 586347-25-3 ZCAPLUS

CN Benzamide, N-[[4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-

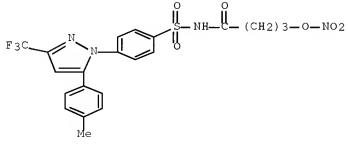
yl]phenyl]sulfonyl]-4-[(nitrooxy)methyl]-, sodium salt (1:1) (CA INDEX NAME)



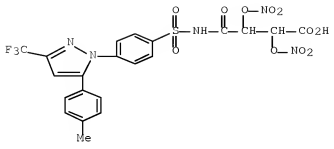
RN 586347-39-9 ZCAPLUS
CN Butanamide, N-[[4-(5-methyl-3-phenyl-4-isoxazolyl)phenyl]sulfonyl]-4-(nitrooxy)- (CA INDEX NAME)



RN 586347-45-7 ZCAPLUS
CN Butanamide, N-[[4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]phenyl]sulfonyl]-4-(nitrooxy)- (CA INDEX NAME)

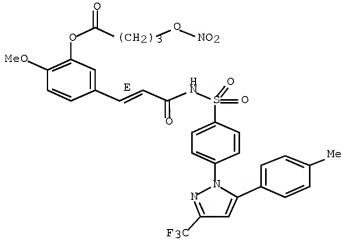


RN 586347-46-8 ZCAPLUS
CN Butanoic acid, 4-[[[4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]phenyl]sulfonyl]amino]-2,3-bis(nitrooxy)-4-oxo- (CA INDEX NAME)



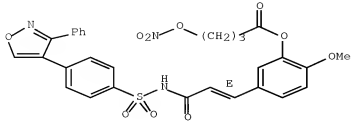
RN 586347-47-9 ZCAPLUS
CN Butanoic acid, 4-(nitrooxy)-, 2-methoxy-5-[(1E)-3-[[[4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]phenyl]sulfonyl]amino]-3-oxo-1-propen-1-yl]phenyl ester (CA INDEX NAME)

Double bond geometry as shown.



RN 586347-48-0 ZCAPLUS
CN Butanoic acid, 4-(nitrooxy)-, 2-methoxy-5-[(1E)-3-oxo-3-[[[4-(3-phenyl-4-isoxazolyl)phenyl]sulfonyl]amino]-1-propen-1-yl]phenyl ester (CA INDEX NAME)

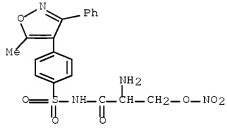
Double bond geometry as shown.



RN 586347-50-4 ZCAPLUS
CN Propanamide, 2-amino-N-[[4-(5-methyl-3-phenyl-4-isoxazolyl)phenyl]sulfonyl]-3-(nitrooxy)-, nitrate (1:?) (CA INDEX NAME)

CM 1

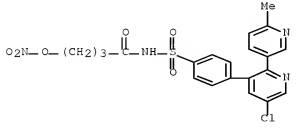
CRN 586347-49-1
CMF C19 H18 N4 O7 S



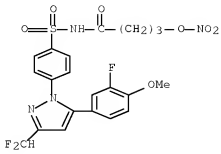
CM 2

CRN 7697-37-2
CMF H N O3

RN 586347-57-1 ZCAPLUS
CN Butanamide, N-[[4-(5-chloro-6'-methyl[2,3'-bipyridin]-3-yl)phenyl]sulfonyl]-4-(nitrooxy)- (CA INDEX NAME)

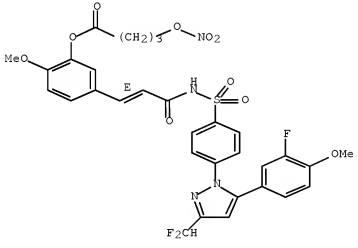


RN 586347-62-8 ZCAPLUS
CN Butanamide, N-[[4-[3-(difluoromethyl)-5-(3-fluoro-4-methoxyphenyl)-1H-pyrazol-1-yl]phenyl]sulfonyl]-4-(nitrooxy)- (CA INDEX NAME)



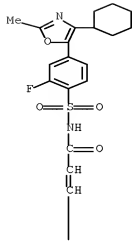
RN 586347-63-9 ZCAPLUS
CN Butanoic acid, 4-(nitrooxy)-, 5-[(1E)-3-[[[4-[3-(difluoromethyl)-5-(3-fluoro-4-methoxyphenyl)-1H-pyrazol-1-yl]phenyl]sulfonyl]amino]-3-oxo-1-propen-1-yl]-2-methoxyphenyl ester (CA INDEX NAME)

Double bond geometry as shown.

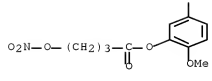


RN 586347-65-1 ZCAPLUS
CN Butanoic acid, 4-(nitrooxy)-, 5-[3-[[[4-(4-cyclohexyl-2-methyl-5-oxazolyl)-2-fluorophenyl]sulfonyl]amino]-3-oxo-1-propen-1-yl]-2-methoxyphenyl ester (CA INDEX NAME)

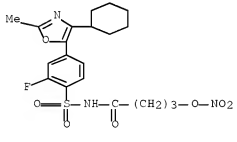
PAGE 1-A



PAGE 2-A



RN 586347-66-2 ZCAPLUS
CN Butanamide, N-[[4-(4-cyclohexyl-2-methyl-5-oxazolyl)-2-fluorophenyl]sulfonyl]-4-(nitrooxy)- (CA INDEX NAME)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 6 OF 6 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:1396034 ZCAPLUS Full-text
DOCUMENT NUMBER: 148:33758

TITLE: Nitrated heterocyclic compounds as endothelin receptor antagonist and their preparation, pharmaceutical compositions and use in the treatment of diseases

INVENTOR(S): Almirante, Nicoletta; Biondi, Stefano; Ongini, Ennio
PATENT ASSIGNEE(S): Nicox S.A., Fr.

SOURCE: PCT Int. Appl., 251pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007137980	A1	20071206	WO 2007-EP55012	20070523
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2007267209	A1	20071206	AU 2007-267209	20070523
CA 2652636	A1	20071206	CA 2007-2652636	20070523
EP 2021324	A1	20090211	EP 2007-729447	20070523
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS				
KR 2009020559	A	20090226	KR 2008-726471	20081029
MX 2008015289	A	20081212	MX 2008-15289	20081128
IN 2008CN06766	A	20090327	IN 2008-CN6766	20081208
NO 2008005375	A	20090225	NO 2008-5375	20081223

PRIORITY APPLN. INFO.: EP 2006-114617 A 20060529
WO 2007-EP55012 W 20070523

OTHER SOURCE(S): MARPAT 148:33758

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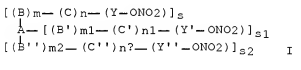

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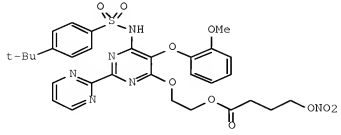
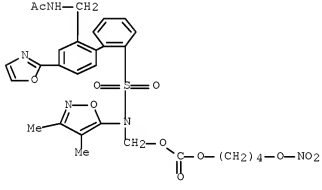


II

AB Endothelin receptor antagonist nitro derivs. of general formula I having an improved pharmacol. activity compared with their parent compds. They can be employed for treating or preventing endothelial-related disorders, renal, pulmonary, cardiac and vascular diseases, and inflammatory processes. Compds. of formula I wherein m, m1, m2, n, n1, n2, s, s1 and s2 are 0 and 1; A is substituted pyrimidinyloxyalkanol, substituted pyrimidinyloxyalkyloxy, etc.; B, B' and B'' are CO, CO2 and CONH; C, C' and C'' are CH(CH3)OCO2, CH2OCO2, and C(CH3)2OCO2; and their pharmaceutically acceptable salts and stereoisomers thereof, are claimed. Example compound II was prepared by transesterification of 4-(nitrooxy)butanoic acid pentafluorophenyl ester with Bosentan. All the invention compds. were evaluated for their endothelin receptor antagonistic activity. From the assay, it was determined that compound II exhibited EC50 value of 33.9 ± 2.5 μM.

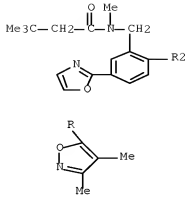
IT 959639-10-2P 959639-11-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of nitrated heterocyclic compds. as endothelin receptor antagonist useful in the treatment of diseases)

RN 959639-10-2 ZCAPLUS
CN Carbonic acid, [[[2'-[(acetylamino)methyl]-4'-(2-oxazolyl)[1,1'-biphenyl]-2-yl]sulfonyl](3,4-dimethyl-5-isoxazolyl)amino]methyl 4-(nitrooxy)butyl ester (CA INDEX NAME)



RN 959639-11-3 ZCAPLUS
CN Carbonic acid, [(3,4-dimethyl-5-isoxazolyl)[[2'-[[(3,3-dimethyl-1-oxobutyl)methylamino]methyl]-4'-(2-oxazolyl)[1,1'-biphenyl]-2-yl]sulfonyl]amino]methyl 4-(nitrooxy)butyl ester (CA INDEX NAME)

PAGE 1-A



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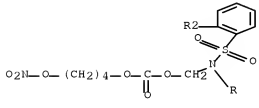

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> d his full

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     FILE 'REGISTRY' ENTERED AT 14:46:27 ON 07 MAY 2009
L1                STRUCTURE UPLOADED
L2              2 SEA SSS SAM L1
                  D SCA
L3                STRUCTURE UPLOADED
L4              2 SEA SSS SAM L3
                  D SCA
L5             31 SEA SSS FUL L3
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L6              6 SEA SPE=ON  ABB=ON  PLU=ON  L5

     FILE 'REGISTRY' ENTERED AT 14:53:50 ON 07 MAY 2009

     FILE 'BEILSTEIN' ENTERED AT 14:54:59 ON 07 MAY 2009
L7              0 SEA SSS SAM L3
L8              0 SEA SSS FUL L3

     FILE 'WPIX' ENTERED AT 14:55:30 ON 07 MAY 2009
L9              4 SEA SSS SAM L3
L10            21 SEA SSS FUL L3
L11             5 SEA SPE=ON  ABB=ON  PLU=ON  L10/DCR

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                  SAVE TEMP L10 BIA938WPIX3L/A

     FILE 'STNGUIDE' ENTERED AT 14:57:28 ON 07 MAY 2009

     FILE 'ZCAPLUS, WPIX' ENTERED AT 14:58:40 ON 07 MAY 2009
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     FILE 'REGISTRY' ENTERED AT 15:00:02 ON 07 MAY 2009
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                  D SCA

     FILE 'ZCAPLUS' ENTERED AT 15:00:37 ON 07 MAY 2009
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L15           246 SEA SPE=ON  ABB=ON  PLU=ON  DELSOLDATO P?/AU OR DEL SOLDATO
                  P?/AU
L16            54 SEA SPE=ON  ABB=ON  PLU=ON  SANTUS G?/AU
L17            13 SEA SPE=ON  ABB=ON  PLU=ON  L15 AND L16
L18           490 SEA SPE=ON  ABB=ON  PLU=ON  NITROOXY?/BI
L19           115 SEA SPE=ON  ABB=ON  PLU=ON  NITRO OXY?/BI
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L25             2 SEA SPE=ON  ABB=ON  PLU=ON  L17 AND (L23 OR L24)
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               D STAT QUE L6

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               D STAT QUE L8

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               D STAT QUE L11

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L32            6 DUP REM L6 L8 L11 (5 DUPLICATES REMOVED)
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               D IBIB ABS HITSTR L32 1-6


     FILE HOME

     FILE REGISTRY
     Property values tagged with IC are from the ZIC/VINITI data file
     provided by InfoChem.

     STRUCTURE FILE UPDATES:    6 MAY 2009  HIGHEST RN 1143575-54-5
     DICTIONARY FILE UPDATES:   6 MAY 2009  HIGHEST RN 1143575-54-5

     New CAS Information Use Policies, enter HELP USAGETERMS for details.

     TSCA INFORMATION NOW CURRENT THROUGH January 9, 2009.

       Please note that search-term pricing does apply when
       conducting SmartSELECT searches.

     REGISTRY includes numerically searchable data for experimental and
     predicted properties as well as tags indicating availability of
     experimental property data in the original document.  For information
     on property searching in REGISTRY, refer to:

     http://www.cas.org/support/stngen/stndoc/properties.html

     FILE ZCAPLUS
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FILE COVERS 1907 - 7 May 2009 VOL 150 ISS 19
FILE LAST UPDATED: 6 May 2009 (20090506/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2009

ZCAplus now includes complete International Patent Classification (IPC)
reclassification data for the third quarter of 2008.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate
substance identification.

FILE BEILSTEIN
FILE LAST UPDATED ON April 1, 2008

FILE COVERS 1771 TO 2008.
FILE CONTAINS 10.322,808 SUBSTANCES

>>>PLEASE NOTE: Reaction Data and substance data are stored in
separate documents and can not be searched together in one query.
Reaction data for BEILSTEIN compounds may be displayed
immediately with the display codes PRE (preparations) and REA
(reactions). A substance answer set retrieved after the search
for a chemical name, a compounds with available reaction
information by combining with PRE/FA, REA/FA or more generally
with RX/FA. The BEILSTEIN Registry Number (BRN) is the link
between a BEILSTEIN compound and belonging reactions. For mo
detailed reaction searches BRNs can be searched as reaction
partner BRNs Reactant BRN (RX.RBRN) or Product BRN (RX.PBRN).<<<

>>> FOR SEARCHING PREPARATIONS SEE HELP PRE <<<

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*************************************************************
* PLEASE NOTE THAT THERE ARE NO FORMATS FREE OF COST.       *
* SET NOTICE FEATURE: THE COST ESTIMATES CALCULATED FOR SET NOTICE *
* ARE BASED ON THE HIGHEST PRICE CATEGORY. THEREFORE; THESE *
* ESTIMATES MAY NOT REFLECT THE ACTUAL COSTS.               *
* FOR PRICE INFORMATION SEE HELP COST                       *
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>>> Price change as of January 1st, 2008: Connect Time and Structure
Search fees re-introduced. See NEWS and HELP COST <<<

FILE WPIX
FILE LAST UPDATED: 7 MAY 2009 <20090507/UP>
MOST RECENT UPDATE: 200928 <200928/DW>

DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE
>>> Now containing more than 1.3 million chemical structures in DCR <<<

>>> IPC, ECLA and US National Classifications have been updated
with reclassifications to March 15th, 2009.
F-Term and FI-Term original classifications are current and
reclassification will commence in June.
No update date (UP) has been created for the reclassified
documents, but they can be identified by
specific update codes (see HELP CLA for details)<<<

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PLEASE VISIT:
http://www.stn-international.com/stn_guide.html

FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
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http://www.stn-international.com/DWPIAnaVist2_0608.html

>>> HELP for European Patent Classifications see HELP ECLA, HELP ICO <<<

FILE STNGUIDE
FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: May 1, 2009 (20090501/UP).

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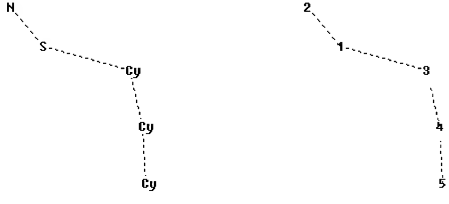

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exact/norm bonds :
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Connectivity :
2:2 M minimum RC ring/chain
Match level :
1:CLASS  2:CLASS  3:Atom  4:Atom  5:Atom  6:CLASS  7:CLASS  8:CLASS  9:CLASS


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